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CARDIOLOGICAL PRACTICE IN THE ERA OF CARDIAC SURGERY WITH PUMP-OXYGENATORS (BYPASS CARDIOLOGY)*†

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TO HAVE been asked to deliver the first John Palmer Lecture as a memorial to this physician, one of the founders of the Canadian Heart Association and a significant contributor to cardiological knowledge, is indeed an honour. Dr. Palmer¹ did not have many medical forebears but one of his grandfathers founded the Prince Edward Island Hospital in Charlottetown, and his portrait hangs in the lobby of that hospital. Dr. Palmer himself, according to a brother, always wished to be a physician, and when 13 years of age observed an operation performed on this brother. As a student in London myself in 1939, I became familiar with the work that Dr. Palmer accomplished on the prognosis for patients with myocardial infarction,² when he was with Sir John Parkinson. You, in this audience, are more familiar with the day-to-day work of Dr. Palmer than I. It interested me to learn of his quiet efficiency in the evacuation of his forces from a torpedoed ship during the last war, of his many interests outside medicine, and of his spending the day before his death at the exhibition of Sir Winston Churchill's paintings.

His medical interests, as revealed by his publications, make it particularly fitting that this lecture should deal with recent surgical contributions to cardiology. He belonged to the workers on the frontier in this field, supporting the surgical work on coronary insufficiency being carried out in this city.³ I should like to quote Dr. Palmer's prophetic statements made in 1947:⁴ "It is possible that some day somebody may devise an artificial valve . . . a

prerequisite would of course be the development of some means of sidetracking the bloodflow during the operation." Incidentally, too, mention should be made of the propriety of holding a symposium on the remarkable cures of patients with congenital heart disease today in this city where for many years Dr. Maude Abbott kept alive an interest in congenital heart disease, to which so many physicians were so long apathetic.

The main problem of the practising cardiologist in the present period of surgical progress is the difficulty in keeping abreast of the surgeon as the latter makes rapid strides forward in the treatment of conditions which the conservative, or even so-called logically minded, physician would have thought inoperable. As a title to this lecture, thinking of the merit of brevity, I had thought of "Bypass Cardiology", and I cannot resist the temptation of making a play on the words in that the surgeon, proud of his advances and perhaps fretting with the conservatism of some of his cardiological confreres, might regard this era as being properly designated as one of "cardiologist bypass".

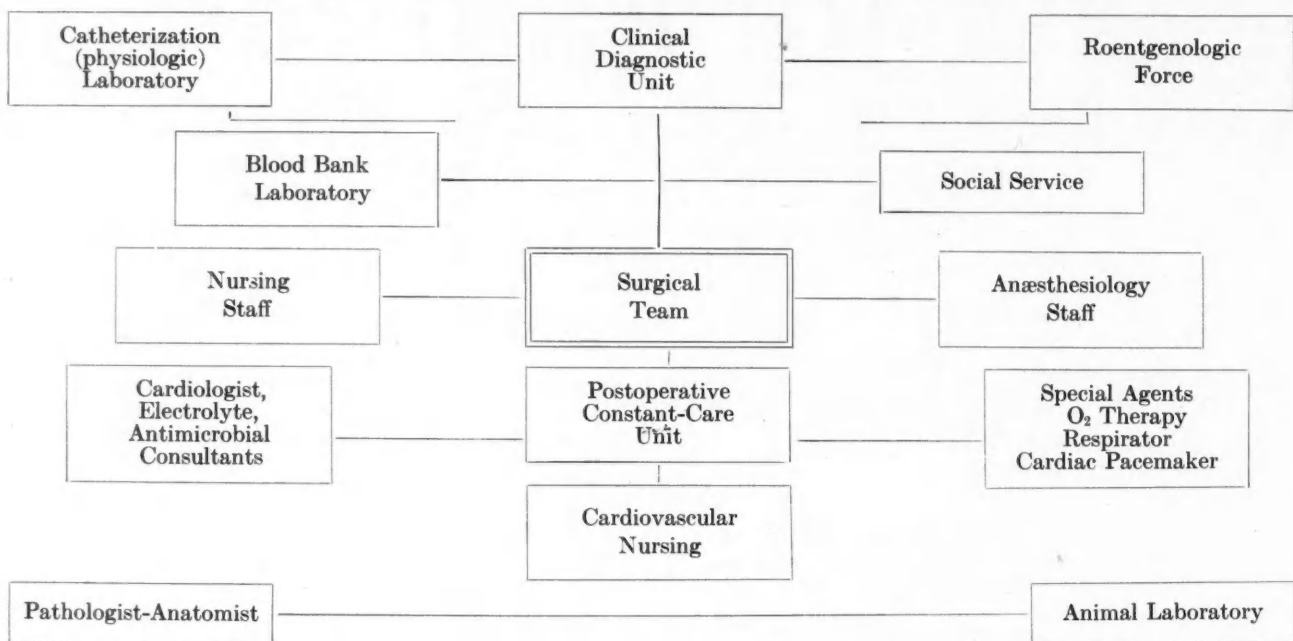
In all sobriety, however, the surgeon would be the first to emphasize the necessity of the team approach in the surgical treatment of cardiac problems utilizing a pump-oxygenator. For support of the medical point of view, I may quote again from Dr. Palmer:⁴ "It goes without saying that in this, as in so many other specialties, a close and harmonious liaison must be maintained between physician and surgeon." Besides the team in the surgical theatre (Table I), the surgeon must have some confidence in the group that helps in the selection of cases, in the laboratory for the necessary supply of blood of the proper type, in the social service group to make certain that the economic needs of the patient and relatives are, in part at least, satisfied, and in those with skill and training in the special diagnostic and roentgenological facilities that may be necessary to give support in depth to the occasionally indicated difficult diagnostic procedures. The anaesthesia staff must be one that has special physiological knowledge and special training in the field. Following the patient's operation, at the Mayo Clinic we judge important a special nursing constant-care area, and in our enterprise the patients usually

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TABLE I.—GROUPS AND AGENTS MAKING CONTRIBUTIONS TO SUCCESSFUL CARDIAC OPERATIONS



stay in the special nursing area for two to four days. The unit takes care of patients in this period regardless of the age of the individual. Organized facilities and trained personnel with special knowledge must be available to make certain that any equipment such as oxygen tents and apparatus for assisted respiration and aerosol inhalation is utilized properly. Postoperative complications are rare, and more details of the strategic approach in their prevention or early amelioration will be found in reports of the surgical group.

CLINICAL PROBLEMS

Just two years ago I was privileged to give the Henry Jackson Lecture⁵ with the title of "Clinical Problems Related to Surgical Repair of Intracardiac Defects with the Aid of an Extracorporeal Pump-Oxygenator". The problems of today are essentially the same although the experience at the Mayo Clinic has been expanded to encompass approximately 780 cases as of the end of May this year.

In principle, the cardiologist helping to select patients for operation is confronted with two problems: that of accurate diagnosis and that of prognosis. For decades it has been recognized that cardiologists may be better diagnosticians than they are prognosticians, and it is in the latter area that the surgeon may become justifiably impatient with their shortcomings. If one can neither give an accurate prognosis nor cure the patient, then the surgeon may believe that a try at repair may be worth while. The error in logic is that the surgeon and the cardiologist should be able to compare prognoses, or to balance the risks, with and without surgery. It is self-evident that the objective of the surgical treatment must be clear and specific; that is, whether it is for cure or

palliation. Implicit in this philosophy is the axiom that a greater immediate risk may be accepted when the objective is cure than when it is palliation alone.

Regarding diagnosis, the cardiologist may perform a useful service in recognizing secondary defects or complications which are in the background of the primary, or obvious, defect. In diagnostic skill, the surgeon perhaps has not quite caught up with the internist in the use of the stethoscope or the recognition of second and third derivative diagnoses, that is, the complications of the complications. For example, the internist may be able to draw attention to the presence of valvular deficiency in patients with ventricular septal defect, and to deformities in the region of the atrioventricular valve in patients with clinical atrial septal defect. We have included in the category of deformities of the atrioventricular canal those which commonly are indexed under the term of "ostium primum defects". The recognition of defects of the atrioventricular cushion area from the electrocardiogram alone is remarkably accurate. Since the beginning of 1956, none out of the 151 patients operated on for the usual type of atrial septal defect at the clinic has proved to have an ostium primum defect.⁶ The differentiation from the electrocardiogram between a ventricular septal defect and atrioventricular canal defects is less accurate, but still about 90% discrimination may be achieved. Emphasis should be placed on the utilization of all the data available for diagnosis and the need for fitting all the pieces of information into the picture. As soon as any clinician becomes a slave of one technique or tends to ascribe an absolute value to a test, he will be following an inexorable course toward making a humiliating error.

Besides his role in diagnosis and prognosis as related to the selection of cases for operation, the cardiologist should contribute to the objective evaluation of the surgical therapy. This indeed is a responsibility that cannot be shelved and that has been recently re-emphasized by Winchell.⁷ "Bypass cardiology" has given new impetus to the growth of the subspecialty of paediatric cardiology, and the number of paediatricians who are specially trained as diagnosticians and research workers in congenital cardiac disease has increased substantially.

Psychic repercussions.—The psychic repercussions of surgical treatment within the heart, on the patient and the relatives, are not always appreciated. Certainly, the intimate relation that the surgeon may acquire, having had his hands inside the heart of the patient, and its potential symbolic meaning must be remembered. From biblical times, the heart always has been the site of qualities most sought after in man's lofty aspirations, particularly courage and love. In respect to children, I have noted that the attitude of different parents varies markedly when operation is recommended. It swings from one extreme, where the parents do not wish to accept any risk whatsoever, demand unreasonable guarantees of survival and cure, and arrive at an impasse, or refusal of surgery, to the other extreme, where the parents seem unconsciously to push the child toward surgery even when the risk is tremendous, with an attitude suggesting even the sacrificing of the child for easement of the burden of care or, indeed, as an Isaac to be offered as a sacrifice to science. The same problems of course may be evident in the spouse or relative of an adult patient.

Present attitude and problems.—At present proper orientation toward bypass surgery demands acceptance of the fact that the procedure of maintaining the circulation of the body for a considerable period, up to one to two hours, is without risk other than that associated with any major operation requiring anaesthesia. Thus the procedure of bypass, *per se*, is no longer on trial, as regards mortality related to cardiac surgery utilizing the heart-lung oxygenator and carried out in a centre with experienced personnel. The mortality is related to the seriousness of the circulatory disorder before operation and the extent to which the surgeon is able to construct a structurally and functionally normal heart. Thus, one would not expect mortality related to the repair of such defects as pulmonary stenosis and aortic stenosis, when these are valvular and the technical result is good, or of atrial septal defects under direct vision, and this is virtually the fact. The experience at the Mayo Clinic dating from March 1955, and now involving nearly 800 cases, is that the over-all mortality rate is approximately 20%. In the last 100 cases of ventricular septal defect, the mortality rate has been approximately 12%.

Problems still remain to be solved and complications still need to be avoided; those related to pulmonary vascular change are paramount. For those who are interested in the detailed problems of whole-body perfusion and pump-oxygenator evaluations, I refer you to an article from the surgical-anaesthesiologist team.⁸ For historic and special technical developments of the pump-oxygenator, the Harvey and Connor lectures by Gibbon^{9, 10} can be recommended.

It is proper to mention that for the majority of patients operated on at the Mayo Clinic what is called "normal" or "high flow perfusion" has been used, and the oxygenator employed has been a modified version of the original Gibbon type, namely, a vertical screen oxygenator with pumps of the DeBakey type. At present, physiological variables are not continuously monitored. When cardiac arrest is indicated, it is now carried out by cutting off the flow of blood into the coronary arteries and thus producing anoxic arrest. It is doubtful whether any cardiologist a few years ago would have predicted that this would be an excellent way of producing reversible arrest. If the procedure is protracted, perfusion of the coronary vessels is allowed to recur transiently at intervals of 10 to 15 minutes. Haemolysis and metabolic acidosis have not been problems when perfusion is adequate. In the rare patient, usually one who has marked polycythemia, a bleeding diathesis has occurred during operation and in the immediate postoperative period; the nature of the defect in such cases is not understood completely. The possibility of citrate intoxication has been excluded. Renal function and adequate urine formation after operation have presented no serious problem. For knowledge of the specialized minutiae of the surgical procedures that are so important for success, I refer you to the articles indexed under the names of our surgical group, namely, Drs. Kirklin, Ellis and McGoon.

Diagnosis.—In diagnosis the cardiological force can depend largely on their own hands and ears, supplemented by roentgenograms and electrocardiograms of routine type. Occasionally a phonocardiogram may be helpful, particularly when the case is being utilized in a teaching clinic. With no more than the information that can be gleaned from these simple methods, the diagnosis should be made accurately in the majority of cases, and indeed, of the cases in which diagnosis is not made by use of these methods, a considerable number will remain undiagnosed, even after complete investigation by cardiac catheterization and angiocardiology. It is extremely important, however, not to let one's clinical diagnostic ambitions run unbridled; suspicion must be high that occult defects may be lurking in the background and that quantitative laboratory data are often necessary to permit the successful selection of cases for surgical treatment.

In our clinic, children with the diagnosis of ventricular septal defect usually do not undergo any special procedures before surgical treatment; perhaps one of 10 will have cardiac catheterization. In many instances the ear oximeter may be of value. Thus in the electrocardiographic findings, the roentgenological appearance of the pulmonary vasculature and the oximetric determination of the oxygen saturation of arterial blood during rest and exercise we have a stable diagnostic triad. A large percentage of patients with tetralogy of Fallot also may be sent to surgery, with the diagnosis to be later confirmed, without special procedures being carried out. By far the majority of adults referred for intracardiac surgery will have undergone cardiac catheterization; this difference is largely related to the ease with which this procedure is accomplished in adults.

THE VARIOUS SURGICAL DEFECTS

Ventricular septal defects.—The main problems in the surgical treatment of ventricular septal defect outside the technical ones, I believe, are now largely those related to pulmonary hypertension^{11, 12} and advanced pulmonary vascular resistance. When a patient has a moderate-to-large, left-to-right shunt, the indication for treatment is clear-cut and the result may be expected to be good. When the left-to-right shunt is very small and is associated with equal pressures in the two ventricles or when there is a bidirectional shunt, the advisability of operation is always questionable. It seems justifiable to accept the patient with pulmonary hypertension and a small left-to-right shunt for operation, even though the future course of such individuals has not been established as yet. It is expected that postoperatively the pulmonary vascular resistance will still be high and pulmonary hypertension of significant degree will persist. With the possible exception of one case, the early follow-up results indicate, however, that pulmonary hypertension does not progress and, indeed, that it may regress. Laboratory data¹⁰ pertaining to the successful repairs in the cases with high pulmonary vascular resistance at the clinic have not accumulated sufficiently to mirror our total experience, but it seems established now that the five-year or even possibly the ten-year results, rather than the one-year results, will be the interesting ones. I believe that the experience of the group at the University of Minnesota is in accord with this view. Dr. Adams,¹³ in a personal communication, stated that in the 57 patients they have catheterized, an average of 1.8 years after operation, pulmonary vascular resistance as calculated from the flow and pressure usually has not changed significantly.

Our group has previously emphasized that the electrocardiogram may reflect the presence of a left-to-right shunt with singular accuracy. In a recent study, DuShane, Weidman and Branden-

burg¹⁴ found that when the preoperative electrocardiogram was interpreted as revealing evidence of left ventricular overwork, studies in the operating room showed that a drop in pulmonary pressure followed repair of the defect in practically every case. When the preoperative electrocardiogram was not so interpreted, the pulmonary artery pressures usually did not drop when the defect was closed. The latter subgroup contained only 10 cases. This small number of cases in which operation was performed without electrocardiographic evidence of left ventricular overwork reflects the fact that few patients with such electrocardiographic findings were believed to have operable lesions, the selection for operation being supported in this group by other data such as the vascularity of the lungs, the estimation of the cardiac activity by palpation and often the findings at cardiac catheterization.

In physiological studies we have emphasized the important effect of breathing a high concentration of oxygen in the reduction of pulmonary vascular resistance and increasing the left-to-right shunt in patients with ventricular septal defect, but this has not been utilized in an organized fashion in the assessment of operability. As a selective tool, this is true also of studies with infusions of acetylcholine. Such data will be of value when the late postoperative catheterization data are analyzed and compared with the preoperative data. The studies of Shepherd and associates¹⁵ indicate that the mechanism underlying drop in pressure caused by the breathing of 100% oxygen, and incidentally the drop in vascular resistance, is not the same as that triggered by acetylcholine. The mechanisms seem different in nature and also they may be additive. Of illustrative interest is one case of a severe pulmonary hypertension with coarctation, a large ductus opening below the coarctation, and ventricular septal defect. Surgery was planned in two stages, but five months after repair and reconstruction of the aorta with occlusion of the ductus, severe pulmonary hypertension equal to systemic pressure was still present. On acetylcholine infusion, however, the pulmonary pressure dropped to about half the systemic pressure, thus indicating that the ventricular septal defect should be relatively small, that is, small enough to produce a significant transventricular gradient. Data analyzed by Savard¹⁶ in our laboratories indicate that it would be less than 1 sq. cm. per square metre of body surface but probably in this child the diameter was little greater than 1 cm.

Tetralogy of Fallot.—The experience in the reconstruction of the heart in tetralogy of Fallot now encompasses about 140 cases, and in the past two years the mortality rate has been about 16%. Considering the severely debilitated state of some of the patients, this seems to be an acceptable figure. The group for whom the risk is high are the infants and the children with a nearly atresic pulmonary orifice. This group may be differentiated in part

by the near-absence of a murmur and severe disability. That national or international accord has *not* been reached in recommendations for the treatment of tetralogy is illustrated by the varied opinions of surgeons discussing the presentation of Kirklin and associates¹⁷ printed recently and by the advice, at slight variance with that of our group, of Gross.¹⁸

The mechanism responsible for death in this group still needs clarification, as the reconstruction within the heart with the closure of the ventricular septal defect and the opening of the outflow tract of the right ventricle and the pulmonary artery has been adequate in recent years. Pulmonary complications, with oedema as a prominent feature, are the chief findings post mortem in the fatal cases, and one is tempted to accept the easy explanation that the left ventricle is inadequate for the imposed burden of carrying the systemic output. I have doubts that such an explanation is valid or adequate and would rather leave the question unsettled, perhaps wishing further investigation to focus on the structure of the lung and the relation of the bronchial arteries to the pulmonary artery and their connections with the capillaries and pulmonary veins.

At present in the severely debilitated, very young patient with the tetralogy of Fallot, it is believed that there is a place for the Blalock-Taussig anastomotic procedure with the plan of carrying out a complete reconstruction in later years. Of pertinence to the problem is the fact that up to May 1959, reconstructive procedures have been carried out at the clinic in 23 patients with Fallot's tetralogy who had had a previous Blalock procedure or procedures, with only three deaths. This experience suggests that the previous anastomotic procedure may actually decrease the risk of complete intracardiac repair and fortify the decision to perform the anastomotic procedure in the type of high-risk case just alluded to.

Atrioventricular canal defects.—In our clinic the term "atrioventricular canal defect" includes, as mentioned above: (1) the low atrial defect with or without significant deformity of the mitral and tricuspid valves (often called the "ostium primum defect") and (2) defects of the septa both above and below the valve. The former is called "the partial form of the common atrioventricular canal (A-V commune)" and the latter "the complete form". The experience with the incomplete form which clinically presents as an atrial septal defect with or without evidence of mitral incompetence has been a rewarding one with a very low mortality rate, as in the series reported by McGoon and associates.¹⁹ The relief of the mitral incompetence by suture of the mitral cleft has been a significant achievement, although one cannot claim that the incompetence has been eradicated completely in all cases. When the defect is of the complete type, with a large ventricular septal defect below a common valve and an atrial communica-

tion above, the results of operation have been disheartening. Out of 15 patients who could be classified as having this defect, only four survived operation. Despite the high risk I recommend the attempt to repair this defect, and the surgeons at the clinic will still accept such patients for treatment. Perhaps improvement in techniques will give a higher salvage rate.

Ventricular septal defect with corrected transposition.—The combination of a ventricular septal defect with transposition of the great vessels is more common than might be expected from the past records of the archives of heart disease. In our clinic there have been 33 proved cases.²⁰ None of the few patients operated on at the clinic have recovered, and this, I believe, is also the experience of the group at the University of Minnesota Hospitals. This surgical experience points out the need for recognizing such defects, since surgical treatment may best be avoided in these cases. Fortunately, the syndrome is usually typical enough, with the picture of the left-to-right shunt, mitral insufficiency and frequently heart block, to make one suspect the lesion, and a selective angiogram of the pulmonary artery or aorta will reveal graphically the true nature of the problem. In a few cases Ebstein's malformation may be present on the left side, and a clue to its presence may be the appearance of a Wolff-Parkinson-White syndrome in the electrocardiogram. From the surgical viewpoint, one of the main technical problems is the insufficiency of the left atrioventricular valve. If a prosthesis could be developed, the arrangement of the muscular structure of the ventricle should lend itself to its emplacement.

Other congenital defects that have been successfully operated on.—Among the gratifying results of surgery in congenital heart disease have been those in patients with congenital pulmonary stenosis, both valvular and infundibular; aortic stenosis, valvular, supra-valvular and infundibular; combined aortic and pulmonary infundibular stenosis; common atrium; high atrial septal defects (superior vena cava or sinus venosus syndrome); total anomalous pulmonary venous drainage and aortopulmonary communications. Our experience with patients with pulmonary stenosis and intact ventricular septum continues to fortify our belief that the majority of patients have infundibular stenosis and that the approach utilizing the pump-oxygenator and direct-vision excision of the obstructive muscle, as well as any valvular stenosis, is the proper one. It is admitted that valvular stenosis occurs alone, and that in the young child, relief of the valvular stenosis may allow involution of the muscular obstructing collar in the infundibular area. The approach that we recommend for attacking the muscular obstruction seems to be justified, in that the risk is so low that deaths are not expected.

The result in the four cases of aortic sinus aneurysm with rupture has been universally good,

and in the one case of ventricular septal defect with gross aortic incompetence there has been dramatic success.

In the difficult complicated cases, hypothermia, deliberately induced during perfusion, may be of great value. This is exemplified by a young boy who had had a previous Potts operation and a resultant pulmonary artery aneurysm, a persisting huge left-to-right shunt and marked enlargement of the heart operated on by Dr. Kirklin. The aortopulmonary communication was closed from inside the pulmonary artery during 12 minutes of complete circulatory arrest made possible by hypothermia. The patient was re-warmed by perfusion during repair of the ventricular septal defect and reconstruction of the right ventricular outflow tract. The convalescence was without complication.

Acquired heart disease.—The surgical relief (or "clinical cure") of gross mitral incompetence, aortic incompetence, and calcareous aortic stenosis, the aneurysms of the proximal part of aorta and atrial tumours may be regarded as established. The proper selection of patients with valvular defects remains a problem, and although the surgical risk is relatively low considering the fact that many of these patients are in severe failure, being properly assessed at around 20%, the permanency of the repair is still doubtful. Ellis and associates²¹ reported the results of operation for mitral insufficiency in 15 cases at the clinic. The results in cases with a sufficiently long follow-up period continue to be promising. Of the 15 patients, three died at the time of operation or in the early postoperative period; one died a few months later; three had been operated on too recently for total evaluation; of the other nine, seven have maintained evidence of improvement, though two of these have shown by haemodynamic studies a suggestive increase of the incompetence again. It is of interest that of these 15 patients, five had ruptured chordae tendineae and none had a heavily calcified valve. In only two was mitral stenosis of mild degree associated. The dramatic result of a new type of repair for mitral incompetence when the cusp is unsupported because of rupture of the chordae tendineae has been described by McGoon.²²

I had believed that a heavily calcified stenotic aortic valve probably would be an inoperable lesion until a valvular prosthesis could be perfected, but it has been demonstrated to me by our surgeons that in certain favourable cases the piecemeal removal of calcium from such valves is possible and will increase mobility, reduce the systolic pressure gradient to insignificance, and allow more adequate closure of the valve, thus relieving some of the aortic insufficiency. Long-term follow-up will be necessary.

For the small group of patients operated on for aortic insufficiency the story is only moderately encouraging, except for specific instances, among which are the two patients who had a fenestration

of the valve near its base related to previous subacute bacterial endocarditis. In these two patients, operated on respectively by Dr. McGoon and Dr. Kirklin, the almost immediate improvement of cardiac function was dramatic, and the operation may be called "curative" and "equivalent" to that of repair of aortic sinus aneurysm with rupture.

POSTOPERATIVE COMPLICATIONS

Heart block is still the most distressing postoperative complication, but in the past year persistent block has developed in only 2% of the patients operated on for ventricular septal defect and 8% of the patients operated on for tetralogy of Fallot by Dr. Kirklin. With the introduction of cardiac arrest during repair, the incidence of heart block increased but in the past year, since the introduction of a new suturing technique, persistent block has occurred in only one of 53 patients with ventricular septal defect and in three of 54 patients with ventricular septal defect and pulmonary stenosis operated on by Dr. Kirklin. The complete experience with heart block, transient or persistent, observed in children with ventricular septal defect operated on by Dr. Kirklin over a four-year period is being analyzed.²³ It is of some interest to note that the longest period of block that has existed before normal sinus mechanism returned was 29 days.

In the medical treatment of heart block, isoproterenol (Isuprel) may still be given a place of value, and if the problem is associated with shock, so that a pressor agent needs to be given intravenously, epinephrine itself may be of value. In the late postoperative period in the years 1955 and 1956, we had sporadically tried molar sodium lactate and adrenocorticosteroids without seeing any dramatic effect, and although I have no evidence that they were valueless, it is doubtful whether they have a useful place in the management of this type of heart block.

It might be expected that Dr. Palmer would have had keen interest in the problem of heart block, since at one time he reported observations on a patient with complete heart block and recurring decay of the idioventricular pacemaker.²⁴

The advance in cardiac pacemakers has been most helpful, and the utilization of direct stimulating wires on the heart also has helped in maintaining a suitable heart rate in the postoperative period. At present in our practice at the clinic, if a patient has had heart block or an episode suspected of being Stokes-Adams syndrome, the heart is driven regularly for several days without repeated attempts to assess the reliability of the intrinsic pacemaker. The rate used in children is usually 110 and in adults 90; these rates have been arbitrarily arrived at from the observation of the early patients' well-being at such rates. It may be mentioned in passing that some children become dependent on the pacemaker if they have been

allowed to have a number of Stokes-Adams episodes when the machine has been turned off. (The resemblance of the lead wires to the umbilical cord may come to mind.) A real panic may be evident when such a test is made, but this has been done less commonly in the last year or so.

Air embolism is still regarded as a threat, but has been considered to constitute no insoluble problem. Two of the patients with mitral valve disease who were operated on at the clinic had convulsions in the postoperative period, which might well be attributed to air embolism, but none have occurred in later cases to date.

In respect of infection, three years ago in 1956 there was a black period when four cases of subacute bacterial endocarditis due to *Pseudomonas pyocyanea* occurred and the machine was found to be the source of infection. Sterilization procedures were promptly altered and with the present technique a recurrence of such a complication seems excluded. In the past year two deaths have been due to staphylococcal bacteraemia and endocarditis. One operation had been for aortic stenosis on a youngster with congenital subaortic stenosis; the other was for mitral valve disease on a middle-aged man with acquired mitral stenosis and insufficiency. In both instances death followed transitory improvement with special antibiotic (vancomycin) treatment.

Postoperative shock has been a problem in an occasional patient and norepinephrine or epinephrine has been the agent utilized. It has been remarkable for me to see a few patients in what might be called "chronic shock" for two or three days still make an excellent recovery.

The careful record of fluid balance kept while the patient is under supervision in the postoperative constant-care unit is noteworthy. An accumulative balance of intake and output is kept, so that it is easy to see at a glance the patient's state in regard to fluids. The amount of fluid given is based on the work of Sturtz and associates,²⁵ and the water intake is sufficiently limited so that the patients usually complain of some unsatisfied thirst, or wish to have more fluid than is allowed in the first 48 hours. It is of interest that no electrolyte disturbance of any magnitude appears; in particular the potassium levels in the serum have remained normal.

Arrhythmias. — Postoperative arrhythmias are common and for the most part benign. Frequently, nodal rhythm is present and, particularly in patients whose atrium has been entered, atrial fibrillation or flutter may occur. It is interesting how relatively infrequent ventricular extrasystoles are, despite the extensive ventriculotomy that may have been done. I know of only one case of fatal ectopic ventricular mechanism; the patient died suddenly late in the postoperative period when ready for dismissal. Apparently the death was related to ventricular tachycardia and probably to its disorganization into ventricular fibrillation. This patient had had

episodes of a ventricular type of tachycardia preoperatively. In the occasional case in which the ventricular activity is irregular because of many extrasystoles, the treatment of choice is intravenous injection of procainamide (Pronestyl), and this is generally satisfactory. Of some interest is the persistent sinus tachycardia some patients exhibit; it has been particularly evident in patients after relief of aortic stenosis. In one patient 12 hours after the surgical relief of a supraaortic stenosis the sinus rate went to 180 and remained between 130 and 140 for a week. It is natural to wonder whether the barostatic mechanism regulating heart rate had been disrupted by the entirely new pulse pressure within the aorta and its branches.

THE USE OF DIGITALIS

Over the past four years the extent to which digitalis has been utilized in the preoperative, operative and postoperative period has varied considerably. It has always been used when the consultant believed failure to be imminent or present, but imminent failure cannot be regarded as having guide lines that are uniformly recognizable. Generally, if the patient has not been in heart failure, he goes to operation without digitalization; then if the heart rate increases during operation or if venous pressure increases, a dose is given, which is calculated to be 25 to 30% less than the total average therapeutic dose that might be given. Administration of digitalis is then continued according to the response of the patient after operation. At present, I believe that most of the patients with pulmonary stenosis are digitalized postoperatively. In the past year I have seen more instances of mild digitalis intoxication, including Wenckebach's block particularly in children, but as such effects have been looked for and recognized, they have been found to be benign. The question has arisen whether the patient after bypass has increased sensitivity to digitalis. Probably the answer may be in the negative, but the possibility has to be entertained.

FOLLOW-UP DATA

At present the follow-up studies that we need most are on patients with severe pulmonary hypertension who have had ventricular septal repair. It has already been indicated that the pulmonary vascular resistance apparently changes slowly,²¹ but while there is evidence that some change may be occurring, some patients with high pulmonary vascular resistances and therefore a high surgical risk will have to be accepted for operation. It would be nice if this were not so, for the over-all surgical mortality for repair of ventricular septal defect could be reduced from the present approximately 12% to less than 5% without difficulty, if patients with high pulmonary vascular resistance were excluded from operation. Follow-up observations on

the fate of prostheses will also be most important, particularly on those utilized as gussets to expand the outflow tract of the right ventricle and root of the pulmonary artery in tetralogy of Fallot. The haemodynamic consequences of pulmonary incompetence will need long-term assessment, benign as it seems at present.

COMMENT

I have attempted to present the cardiologist's or internist's view of the experience at the Mayo Clinic related to the repair of various cardiac lesions under direct vision with the heart bypassed and the body supplied with blood through a pump-oxygenator system. The procedure of bypass is established and may be regarded as without significant risk in itself. In a large group of congenital and some acquired defects, rewarding curative and palliative effects have been achieved. Some congenital defects such as transposition of the great vessels, truncus and single ventricles remain challenging problems and are questionably susceptible to complete surgical cure. In the acquired conditions, coronary disease is an area that we have marked for possible exploitation but have not ventured into as yet. Personally, I am convinced of the logic of recommending the removal of cardiac aneurysms of the saccular type, but none have as yet been removed at the clinic. As a closing statement, I reiterate that the pressing problem for solution in day-to-day practice is that of the pulmonary vascular changes related to the pulmonary hypertension when communication between the two ventricles is large.

REFERENCES

1. PALMER, R. M.: Personal communication to the author.
2. PALMER, J. H.: *Quart. J. Med.*, 6: 49, 1937.
3. FAUTEUX, M. AND PALMER, J. H.: *Canad. M. A. J.*, 45: 295, 1941.
4. PALMER, J. H.: *Ibid.*, 56: 380, 1947.
5. BURCHELL, H. B.: *Circulation*, 16: 976, 1957.
6. SILVER, A. W. AND KIRKLIN, J. W.: Accuracy of diagnosis in surgical cases of atrial septal defect. (Unpublished data.)
7. WINCHELL, P.: Personal communication to the author.
8. KIRKLIN, J. W. et al.: What is adequate perfusion? In: *Extracorporeal circulation*, edited by J. G. Allen, Charles C Thomas, Springfield, Ill., 1958, p. 125.
9. GIBSON, J. H., JR.: *Harvey Lect.*, 53: 186, 1959.
10. *Idem*: *Circulation*, 19: 646, 1959.
11. BURCHELL, H. B.: Regression of pulmonary vascular hypertension after cure of intracardiac defects. In: *Pulmonary circulation*, edited by W. L. Adams and I. Veith, Grune & Stratton, Inc., New York, 1959, p. 245.
12. *Idem*: *Brit. Heart J.*, 21: 255, 1959.
13. ADAMS, P.: Personal communication to the author.
14. DUSHANE, J. W., WEIDMAN, W. H. AND BRANDENBURG, R. O.: Personal communication to the author.
15. SHEPHERD, J. T. et al.: *Circulation*, 20: 381, 1959.
16. SAVARD, M.: Unpublished data.
17. KIRKLIN, J. W. et al.: *J. Thoracic Surg.*, 37: 22, 1959.
18. GROSS, R. E.: *New England J. Med.*, 260: 1047, 1959.
19. MCGOON, D. C., DUSHANE, J. W. AND KIRKLIN, J. W.: *Surgery*, 46: 185, 1959.
20. SCHIEBLER, G. L., DUSHANE, J. W., BURCHELL, H. B., EDWARDS, J. E. AND WOOD, E. H.: Unpublished data.
21. ELLIS, F. H., JR. et al.: *A.M.A. Arch. Surg.*, 79: 222, 1959.
22. MCGOON, D. C.: Personal communication to the author.
23. LAUER, R. M. et al.: Heart block occurring after repair of ventricular septal defect in children. (Unpublished data.)
24. PALMER, J. H.: *Am. Heart J.*, 51: 156, 1956.
25. STURTZ, G. S. et al.: *Circulation*, 16: 988, 1000, 1957.

RÉSUMÉ

Au cours de cette première conférence prononcée à la mémoire du docteur J. Palmer, l'auteur insiste dans le traitement chirurgical des maladies cardiaques sur l'importance de la formation d'une équipe dont tous les membres

connaissent à fond leur spécialité avant de s'attaquer au problème. Cette équipe ne comprend pas uniquement le chirurgien, ses assistants et l'anesthésiste, mais doit aussi inclure le cardiologue responsable du choix des cas, le personnel du laboratoire chargé des différentes déterminations biochimiques ainsi que de l'approvisionnement du sang de remplacement, le personnel du service social et celui du nursing. L'auteur tire son expérience de l'étude d'une série de 780 cas traités à la clinique Mayo. Il prétend que le cardiologue doit résoudre le problème non seulement du diagnostic mais aussi du pronostic qui depuis les progrès récents de la chirurgie cardiaque a revêtu une importance considérable.

Avant d'entreprendre une opération de ce genre il convient d'établir avec autant de précision que possible si elle sera curative ou palliative. La dérivation par cœur-poumon artificiel a marqué l'essor de la cardiologie pédiatrique surtout en ce qui concerne les anomalies congénitales. La chirurgie cardiaque comporte des répercussions psychiques chez le malade et sa famille qu'on ne saisit pas toujours à première vue. Le chirurgien qui a mis ses mains à l'intérieur du cœur d'un patient accomplit un acte dont la portée symbolique rivalise avec la valeur chirurgicale. A l'heure actuelle la chirurgie cardiaque basée sur la dérivation extra-corporelle par pompe-oxygénateur permet de maintenir la circulation pendant des périodes de une à deux heures sans exposer le malade à des risques plus graves que ceux que présentent la grande chirurgie et l'anesthésie. La mortalité qui accompagne ce procédé dépend de la gravité des troubles circulatoires pour lesquels il est employé et aussi de la latitude de qui reste au chirurgien de recréer un cœur de structure et de fonction normales. Dans les derniers cent cas de défaut de cloisonnement inter-ventriculaire le taux de mortalité opératoire s'est élevé approximativement à 12%.

Lorsque les circonstances de l'opération l'exigent, on obtient l'arrêt cardiaque en interrompant la circulation des coronaires produisant ainsi une asystolie anoxique. Le diagnostic est fondé surtout sur l'expérience clinique du cardiologue dans l'emploi de ses oreilles et de ses mains. La radiographie et l'électrocardiographie apportent aussi leur aide. Quelquefois la phonocardiographie peut contribuer à l'enseignement clinique. Ces méthodes permettent d'arriver à un diagnostic précis dans la grande majorité des cas et il est intéressant de noter que les problèmes diagnostiques non résolus de cette manière demeurent habituellement insolubles même avec l'aide du cathétérisme cardiaque et de l'angiocardographie. Dans les cas de défaut du septum interventriculaire l'hypertension pulmonaire semble vouloir se stabiliser après l'intervention et même dans certains cas diminuer d'intensité. Il faudra tout de même une période d'observation de cinq ou dix ans avant de pouvoir se prononcer sur ce point. La diminution de la résistance vasculaire pulmonaire après administration de concentration élevée d'oxygène n'a pas encore été utilisée de façon systématique dans l'évaluation des malades pour la chirurgie. Le mécanisme en jeu dans cette circonstance semble différer de celui par lequel agit l'acétylcholine pour produire le même résultat.

Le taux de mortalité associé à l'intervention dans la tétralogie de Fallot s'est maintenu à Mayo dans les deux dernières années à environ 16%. Ce chiffre ne semble pas excessivement élevé si l'on tient compte de l'état de débilité avancée de certains malades qui furent opérés. Chez les sujets très jeunes et gravement atteints il semble que l'intervention de Blalock-Taussig pour anastomoses devrait être accomplie en premier lieu, quitte à procéder à une reconstruction complète quelques années plus tard. La correction de l'insuffisance mitrale par la suture de la fente mitrale représente une réussite importante même si on ne peut prétendre que cette insuffisance ait été pleinement corrigée dans tous les cas. Lorsque l'anomalie est totale avec un gros défaut du cloisonnement inter-ventriculaire sous une valve commune avec communication interauriculaire superposée, les résultats de l'opération sont décourageants. Cependant l'amélioration des techniques nous permet d'envisager un progrès à l'avenir. Dans les cas de défaut du cloisonnement interventriculaire combiné à une transposition des gros vaisseaux l'intervention chirurgicale n'est pas à recommander. Il importe donc d'en faire un diagnostic précis afin d'éviter que ces malades ne subissent l'intervention.

Parmi les autres anomalies dont la chirurgie a su avoir raison, nous comptons la sténose pulmonaire congénitale valvulaire ou infundibulaire, la sténose aortique orificielle,

supra-valvulaire et infundibulaire, les sténoses aortique et pulmonaire combinées, l'oreillette unique et plusieurs autres. La chirurgie se prête également à la correction de l'insuffisance mitrale avancée, de l'insuffisance aortique, de la sténose aortique calcifiante, des anévrysmes de l'aorte ascendante ainsi que des tumeurs des oreillettes. De toutes les complications post-opératoires le bloc auriculo-ventriculaire est le plus pénible. Depuis l'introduction d'une nouvelle technique de suture ces attaques d'Adams-Stokes sont heureusement moins fréquentes; l'auteur considère l'isoprotérénol comme étant encore le meilleur médicament. Les embolies gazeuses sont encore une menace

mais ne constituent plus un problème insoluble. La stérilisation de l'appareil de dérivation doit être parfaite si l'on désire éviter l'endocardite. Les arythmies post-opératoires sont fréquentes et la plupart du temps bénignes. Dans le cas où elles intéressent les ventricules, l'administration intraveineuse d'amide de procaine donne habituellement satisfaction. La plupart des malades qui présentent une sténose pulmonaire reçoivent de la digitaline avant l'opération. On a déjà demandé si le malade soumis à une dérivation extra-corporelle présentait une plus grande sensibilité à la digitaline; la réponse est probablement négative, quoiqu'on doive en garder la possibilité à l'esprit.

SURGICAL TREATMENT OF AORTIC STENOSIS*

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AORTIC STENOSIS is a treacherous condition, for it produces severe myocardial disease before it produces symptoms. From the date of onset of the first episode of syncope, failure or angina, one half of the patients are dead within two years.¹ Because these symptoms usually appear in an otherwise active and robust individual, it is difficult for the patient and his physician to accept the fact that this is a rapidly progressive lethal condition. For the same reason, these patients are often first seen by the surgeon in an advanced state of their disease.

C. P. Bailey successfully opened a stenotic aortic valve in 1950, by passing an instrument through the wall of the left ventricle into the valve orifice and blindly dilating it; this is called the transventricular method of aortic valvotomy. An alternative blind route through the root of the aorta was later recommended.² It was obvious, with the recent trend toward direct vision surgery of cardiac lesions, that the stenosed aortic valve would be operated upon by an open-heart procedure. A direct vision approach with hypothermia was introduced in 1955.³⁻⁵ In 1956, Lillehei reported the first successful case of aortic stenosis treated with the heart-lung pump.⁶

The experience of the group at the Toronto General Hospital with aortic valve surgery over the period from November 1953 to February 1959 is shown in Table I. Our policy in the past has been to recommend the following method of treatment:

1. Aortic stenosis with calcification in adults: transventricular dilatation.
2. Non-calcified or mildly calcified aortic stenosis in older children and young adults: direct-vision repair with use of the heart-lung pump.
3. Congenital aortic stenosis in children: direct-vision repair with hypothermia.

TABLE I.—METHOD OF SURGERY IN 65 CASES OPERATED UPON FOR AORTIC STENOSIS AT TORONTO GENERAL HOSPITAL UP TO FEBRUARY 1959

	No. of cases
Transventricular.....	59
Aortic valvular stenosis.....	42
Combined aortic stenosis and mitral disease.....	15
Subvalvular stenosis.....	2
Direct vision.....	6
Aortic valvular stenosis.....	4
Subvalvular stenosis.....	2
Total number of cases.....	65

At the present time, surgery of the aortic valve is in a state of change and we are extending our indications for direct-vision repair with cardiac bypass. The purpose of this paper is to present the clinical picture of adult calcific aortic stenosis and the results which may be expected with the transventricular method of treatment. A short section is devoted to the newer open heart techniques.

CLINICAL PICTURE OF ADULT CALCIFIC AORTIC STENOSIS

Stenosis in the region of the aortic valve may be either congenital or acquired. The acquired lesion may result from rheumatic fever or arteriosclerosis. The clinical picture of the disease as seen in 42 adult cases of aortic stenosis operated upon by the transventricular method is reviewed in this section.

Of the patients presenting for operation 42% had a positive history of rheumatic fever (Fig. 2). The majority were men (93%), and the mean age was 43 (Fig. 1).

The first symptoms were usually angina, faintness or syncope, and dyspnoea on exertion. The symptoms progressed rapidly in severity. At the time when these patients presented for operation, their symptoms were dyspnoea on exertion (81%), angina (62%), syncope or dizziness (45%), and symptoms of right heart failure or systemic congestion (24%). Hæmoptysis was uncommon

*From the Toronto General Hospital.

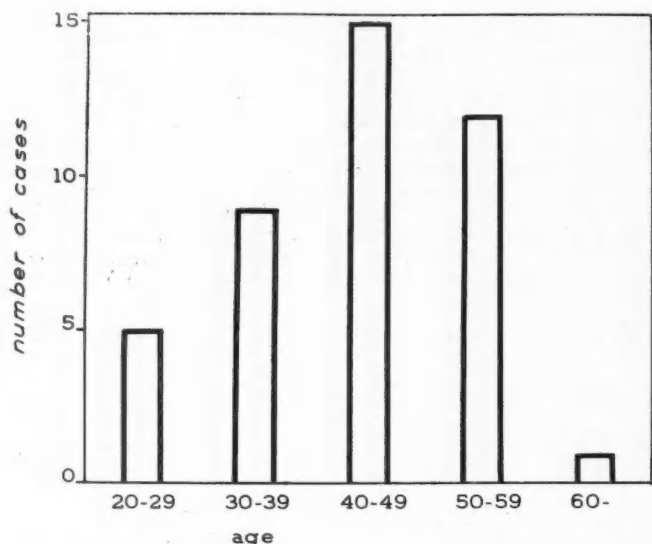


Fig. 1.—The age distribution of 42 patients with pure aortic stenosis operated upon by the transventricular method.

(14%) and systemic emboli were rare (2.4%) (see Fig. 2).

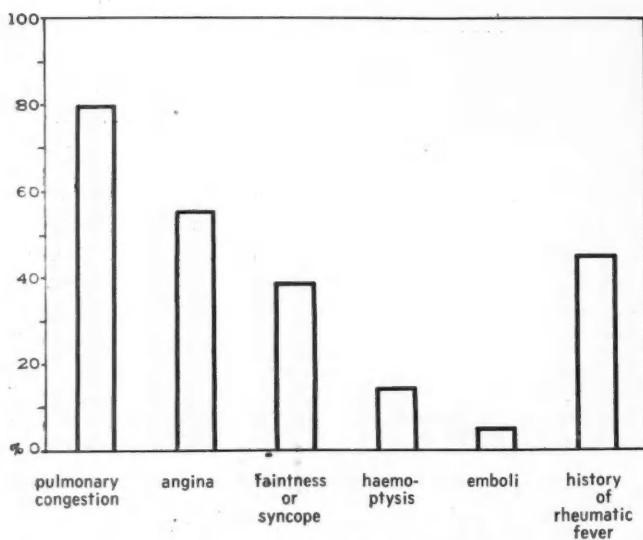


Fig. 2.—Symptoms which had occurred before operation in 42 patients suffering from pure aortic stenosis.

The rapid course of the disease, once symptoms are noted, is well illustrated in the patient shown in Fig. 3. This 52-year-old farmer noted his first symptom just one year before operation. Seven months before operation he was still able to work most of the day at loading hay on to a wagon. His symptoms of angina and dyspnoea on exertion rapidly progressed despite medical treatment and he experienced orthopnoea, paroxysmal nocturnal dyspnoea, ascites and swelling of the ankles. When admitted for operation he was able to walk less than one block at a normal pace. With this one-year history he had progressed to a stage where he was a cardiac invalid in the terminal stages of his disease.

All of the patients had a systolic murmur and this was accompanied by a thrill in over two-thirds. Although a soft aortic diastolic murmur was present

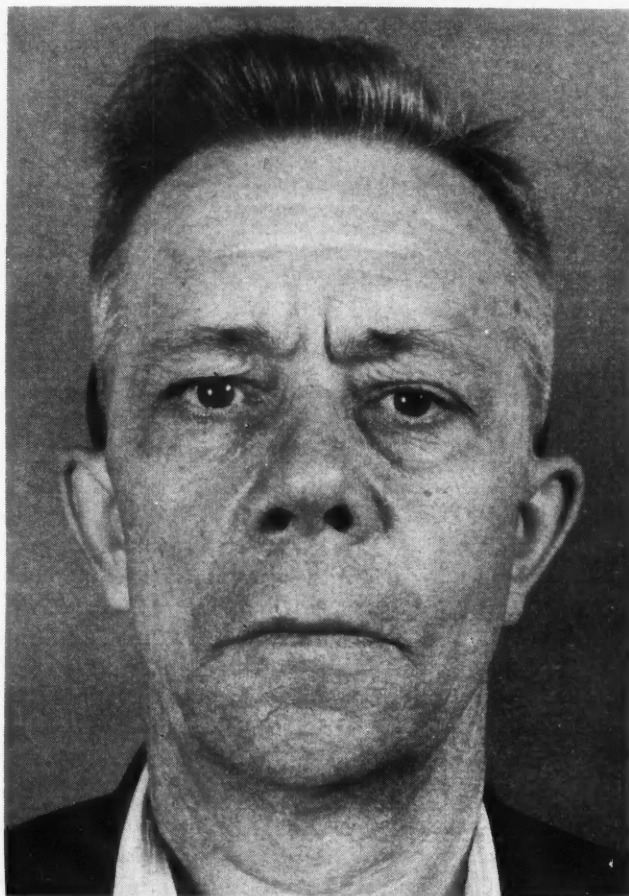


Fig. 3.—At the time of operation this man was unable to walk one block and was in both left and right heart failure. One year previously he was completely free of symptoms. His history illustrates the rapid downhill course of patients suffering from aortic stenosis.

in almost half (48%), none of the patients operated on had significant aortic regurgitation.

The valve was calcified in 94%. In 80% of the cases, signs of left ventricular hypertrophy were present in the electrocardiogram and 20% showed some degree of intracardiac block. Atrial fibrillation is rare in pure aortic stenosis and was present in only one case. Five patients had electrocardiographic changes suggestive of previous myocardial infarction.

PREOPERATIVE INVESTIGATION

The symptoms, physical signs, and the results of x-ray, fluoroscopic and electrocardiographic examination are sufficient to establish a diagnosis of aortic stenosis in most patients. However, in mild or doubtful cases or in cases associated with aortic regurgitation or myocardial or mitral valve disease, special tests are necessary.

Left Heart Catheterization

Catheterization of the left atrium and ventricle by means of a transthoracic left atrial needle puncture under local anaesthesia has been used in 24 cases. A gradient over 50 mm. Hg across the aortic valve during systole is considered significant. The characteristics of the brachial pressure curve (presence of anacrotic notch, delayed upstroke, lengthened systolic period) are of value.

Aortic Reflux Test

If aortic regurgitation is suspected, the aortic reflux test is of value. A cardiac catheter is threaded into the aorta by means of a percutaneous femoral puncture, and Evans blue dye is injected at various levels. The amount of aortic regurgitation is calculated from the level at which dye ceases to pass into the innominate artery and be registered at an oximeter placed on the right ear.

CLASSIFICATION

The symptoms of aortic stenosis are secondary to inadequate circulation to the brain, inadequate circulation to the heart, and myocardial failure. It is our opinion that myocardial failure is the most serious of these symptoms and the one indicating the quickest demise. The patients have been classified into four groups on the basis of their symptoms (Table II).

TABLE II.—CLASSIFICATION OF PATIENTS ON THE BASIS OF THEIR SYMPTOMS

Group 1.....	No symptoms
Group 2.....	Syncopal and/or anginal (may have mild exertional dyspnoea)
Group 3.....	Left heart failure
Group 4.....	Congestive failure

Group 1—No Symptoms

Only one patient was operated upon with signs of the disease only. He had no cardiac symptoms whatsoever. With the very low mortality that can be expected in this group and the known high mortality of the untreated condition, it is probable that in the future patients in this group should be considered for operation.

Group 2—Syncope and/or Angina

The second group of cases consisted of 15 patients suffering from cerebral or myocardial ischaemia who had no signs of left heart failure or, at the most, minimal dyspnoea on exertion.

Group 3—Left Heart Failure

The third group consisted of 16 patients in whom the myocardium of the left ventricle had begun to fail, as evidenced by significant shortness of breath on exertion, orthopnoea, nocturnal dyspnoea or frank pulmonary oedema.

Group 4—Systemic Congestion

The fourth group consisted of 10 patients who had progressed from left heart failure through to the stage of systemic congestion.

OPERATIVE TECHNIQUE

The patients are operated upon in the dorsal position with a sandbag under the left chest and the left arm elevated. The chest is entered through the 5th interspace anteriorly. The pericardial fat

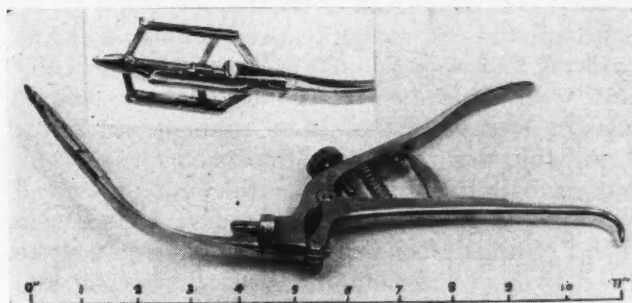


Fig. 4.—The Donaldson transventricular aortic valvulotome in opened (see insert) and closed positions.

is dissected off the fibrous pericardium and retained as a large vascular pad of fat which is applied to the myocardium at the termination of the procedure. The fibrous pericardium is opened widely.

The instrument used in this hospital during recent years has been the Donaldson transventricular aortic valvulotome (see Fig. 4). This instrument has a tri-finned blade and a small blunt tip. After production of a stab wound in the anterior wall of the left ventricle, approximately one and a half inches (3.75 cm.) from the apex and half an inch from the interventricular septum, the instrument is introduced into the interior of the left ventricle. A purse string suture is used to control bleeding. The tip of the instrument is guided through the aortic valve and its position assessed by palpation through the wall of the aorta. Once within the valve orifice, the instrument is opened twice over a distance of one to two inches (2.5-5 cm.) to ensure adequate dilatation of the valve. The head of the dilator is so constructed that when it opens the blades rotate into the natural crevices and rarely produce disruption of a valve leaflet.

Upon withdrawing the instrument from the heart, the ventricular wound is closed by two or three interrupted sutures. During the actual dilatation of the valve, the anaesthetist compresses the carotid arteries to protect the cerebral vessels from calcium emboli.

RESULTS OF SURGERY

Hospital Mortality

Seven of the 42 patients died in hospital—a mortality rate of 16.7%. The mortality varied with the stage of the disease from zero to 40% (see Table III). If the 10 cases which had progressed to Stage 4 were excluded, the hospital mortality was 9.4%. This figure emphasizes the importance of operation early in the course of the disease.

TABLE III.—THE HOSPITAL MORTALITY OF 42 PATIENTS WITH PURE AORTIC STENOSIS OPERATED ON BY THE TRANSVENTRICULAR METHOD

Over-all mortality.....	16.7%
Group 1.....	0%
Group 2.....	7%
Group 3.....	13%
Group 4.....	40%

Only one patient died on the operating table. Four of the six postoperative deaths occurred suddenly and were thought to be due to ventricular fibrillation. In only one of these was a definite calcium embolus found in a coronary artery. It is probable that the greatly thickened myocardium that exists in this disease is on the verge of critical ischaemia at all times. Any period of hypotension in the postoperative period exposes the patient to the danger of transient myocardial ischaemia and ventricular fibrillation. Two patients died from heart failure.

Clinical Improvement of Patients

Thirty-five patients survived the operation and have been followed up over a period which varies from six years to six months (Fig. 5); 21 patients

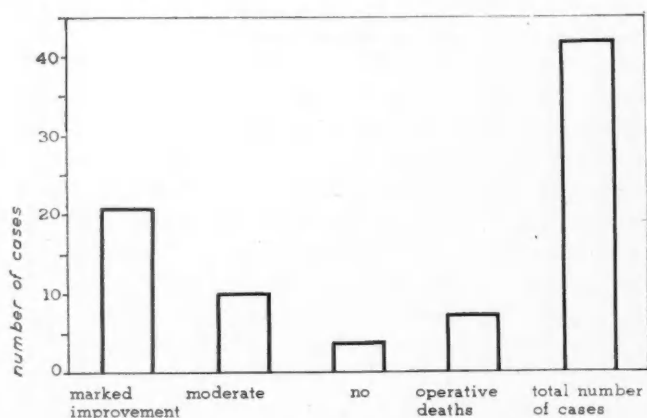


Fig. 5.—Results of surgery of 42 patients with pure aortic stenosis operated on by the transventricular method.

were markedly improved. Most of these patients returned to their normal jobs and all were without significant disability. Ten patients were moderately improved. These patients still had significant disability but there was definite improvement on the preoperative state. Four patients were unimproved by the operation.

Late Deaths

Late deaths have occurred in seven of the 35 survivors. One death was sudden and possibly due to myocardial ischaemia. Five patients died of heart failure. One patient committed suicide. Four of the late deaths occurred in the group which was unimproved by the operation, and the remaining three in the group which was only moderately improved. At the present time, therefore, 28 patients (80%) out of the 35 patients surviving operation are still alive and all are markedly or moderately improved.

Reduction of Gradient

The reduction of the systolic gradient across the aortic valve has averaged 50 mm. Hg (see Fig. 6). These gradients are measured on the operating table and often continue to fall for some time as the heart adjusts to the new size of the valve. The gross narrowing and distortion of the valve and the

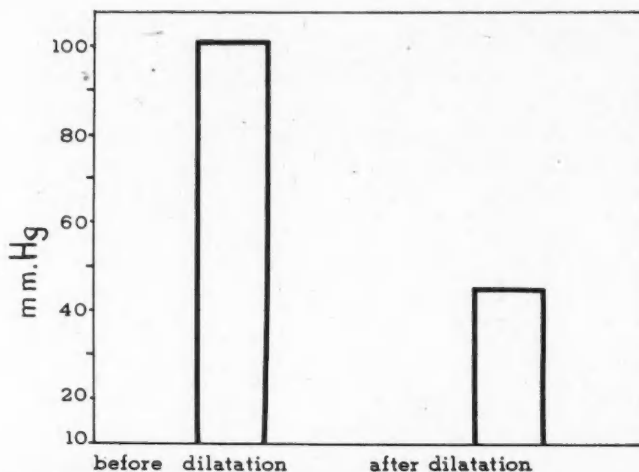


Fig. 6.—Reduction of the systolic gradient across the aortic valve measured on the operating table in 25 cases.

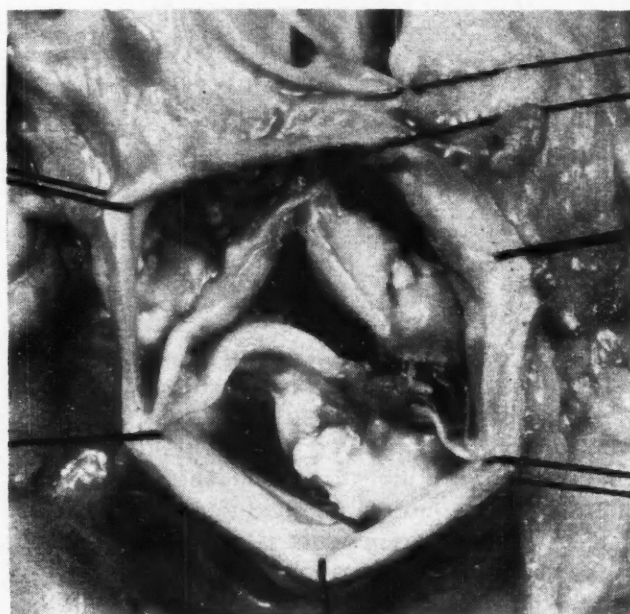


Fig. 7.—A calcified and stenotic aortic valve viewed at autopsy.

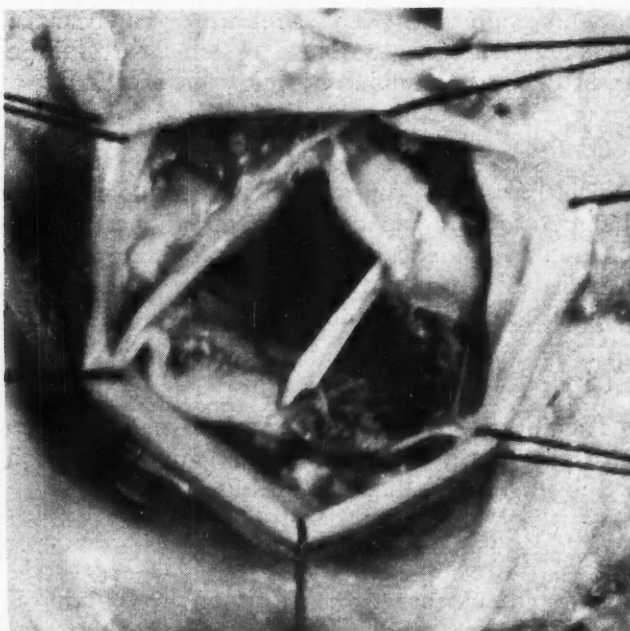


Fig. 8.—The same valve as in Fig. 7 showing the opening obtained at operation by transventricular dilatation. A wooden peg is used to evert the cusps.

result which can be produced by blind dilatation are well illustrated in Figs. 7 and 8.

Aortic Regurgitation

A major danger of any type of operation on the aortic valve is the production of aortic regurgitation. Significant regurgitation (pulse pressure over 60 mm. Hg and diastolic pressure under 60 mm. Hg) has been produced in two of the 42 cases. It is probable that some insignificant aortic regurgitation has been produced in several others.

COMBINED AORTIC AND MITRAL VALVE DISEASE

Patients who develop aortic stenosis and mitral valve disease are a distinctly different group from those with pure aortic stenosis. Eleven of our 15 patients were women, 80% had a positive history of rheumatic fever, and their symptoms were quite different (Fig. 9). The main complaint of these

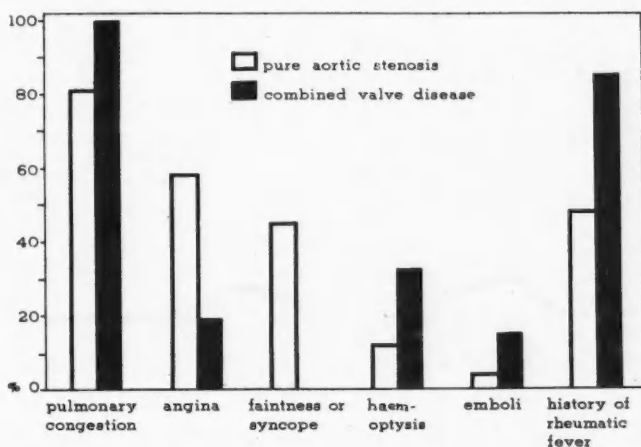


Fig. 9.—Comparison of symptoms present at time of operation in patients with pure aortic stenosis and in those with combined aortic and mitral stenosis.

patients was exertional dyspnoea. Very few had angina and none had symptoms of cerebral ischaemia. Haemoptysis and embolism on the other hand were much more frequent.

Calcium was less often visible in the valve (50%). The electrocardiographic pattern was quite different, fewer cases showing left ventricular hypertrophy (64%) and far more presenting with auricular fibrillation (67%). Their symptoms had been present longer before they appeared for operation. At operation, there was less fat in the epicardium, and the myocardium itself was less streaky and not as thick. The right ventricle appeared to be hypertrophied as well as the left. The systolic gradients across the aortic valve were smaller. A preoperative gradient of 30 mm. Hg was considered significant in a patient with associated mitral stenosis. Two of the 15 patients with combined valvular disease (13.3%) died in hospital. There have been two late deaths among the 13 survivors of the operation (Fig. 10).

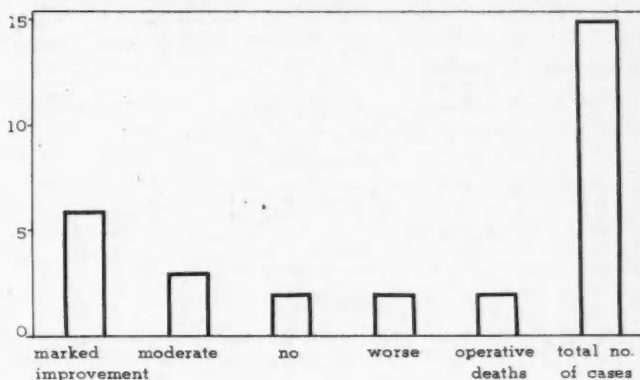


Fig. 10.—The results of surgery in 15 patients with combined mitral and aortic stenosis.

DIRECT VISION SURGERY

Hypothermia

We feel that the gross abnormalities present in the calcified aortic valve of the adult cannot be corrected under direct vision in the eight minutes allowed by present-day hypothermia. In the past, hypothermia was considered adequate for the correction of the congenital non-calcified aortic and subaortic stenosis of children. With the recent improvements in cardiac bypass we have found that the extra time given by the pump is of value even in this group in allowing a more accurate and complete correction.

Heart-Lung Pump

At present the heart-lung pump is being used more frequently for surgery of the stenotic aortic valve. In the non-calcified lesions such as the congenital valvular and subvalvular stenosis of children, it is possible to produce a nearly perfect anatomical and physiological result. Up to February 1959, we have operated upon three such patients and all have survived and done well. In the lightly calcified valve of the younger adult a more complete correction can probably be obtained by this method than by a blind dilatation. Its advantage in the heavily calcified valve is still debatable. In the poor-risk or older patient it is unlikely that it will supplant the blind transventricular procedure.

SUMMARY AND CONCLUSIONS

Sixty-five cases of aortic stenosis operated on at the Toronto General Hospital up to February 1959 are reviewed. Special attention is paid to 42 cases of pure aortic stenosis in the adult operated upon by the transventricular method.

Patients with aortic stenosis run a rapidly downhill course after the onset of symptoms, and early operation is imperative.

The hospital mortality varies with the stage of the disease from zero to 40%. The overall mortality with the transventricular method is 16.7%.

A follow-up of six months to six years reveals that 80% of those leaving hospital are alive with moderate or marked improvement.

In recent months, the indications for operation under direct vision with the aid of the heart-lung pump have been extended.

Drs. D. R. Wilson, J. A. Key and R. O. Heimbecker contributed cases to this series.

REFERENCES

1. BERGERON, J. *et al.*: *A.M.A. Arch. Int. Med.*, **94**: 911, 1954.
2. BAILEY, C. P. *et al.*: *Circulation*, **9**: 22, 1954.
3. JULIAN, O. C. *et al.*: *A.M.A. Arch. Surg.*, **73**: 493, 1956.
4. SWAN, H. AND KORTZ, A. B.: *Ann. Surg.*, **144**: 205, 1956.
5. LEWIS, F. J. *et al.*: *J. Thoracic Surg.*, **32**: 481, 1956.
6. LILLEHEI, C. W. *et al.*: *Dis. Chest*, **30**: 123, 1956.

RÉSUMÉ

En février 1959 on avait opéré 65 cas de sténose aortique à l'hôpital général de Toronto. Au cours de cette revue,

les auteurs attirent l'attention sur 42 cas de sténose aortique pure chez l'adulte, opérés par abord trans-ventriculaire. Les malades atteints de cette affection perdent rapidement du terrain dès la première manifestation des symptômes: il importe donc d'intervenir d'emblée. Le taux de mortalité post-opératoire tel que déterminé pendant le séjour du malade à l'hôpital s'étend de 0 à 40% selon le stage de la maladie. La mortalité totale qui accompagne la méthode trans-ventriculaire se chiffre à 16.7%. L'observation des opérés poursuivie pendant des périodes variant de six mois à six ans montre que 80% de ceux qui dépassent la période post-opératoire critique sont encore en vie et jouissent d'une amélioration moyenne ou prononcée. Les indications opératoires de l'intervention sous le contrôle de la vue grâce au cœur-poumon artificiel ont été récemment étendues.

THE RELATION OF HEART SOUNDS TO LEFT ATRIAL PRESSURE*

CHARLES B. RICH, M.D., F.R.C.P.[C],
F.A.C.P.,† Edmonton, Alta.

FIFTY CASES of mitral stenosis have been studied, to investigate the relationship of heart sounds to left atrial pressure. In all cases, three simultaneous tracings were made: electrocardiogram, phonocardiogram and left atrial pressures (L.A.P.). Nine cases were shown to have added to stenosis a significant degree of insufficiency, and all cases were studied either before or after operation.

The apparatus used was the Electronics for Medicine machine. Left atrial pressures were taken by transbronchial puncture. Where there was any doubt of the position of the first heart sound or the opening snap, a further tracing was taken with the Sanborn Twin Beam using the E.C.G. as a common base line.

In this study, as illustrated in Fig. 1, the R-I interval was measured from the peak of the R wave to the maximal vibration of the first sound. The peak of R was used rather than the beginning of Q, since it is a more definite point and Q was not always present. The second OS interval was measured from the beginning of the big vibrations of the second sound to the beginning of the opening snap. In most cases of pure mitral stenosis, a notch was seen on the Y descent. This we have named the opening snap notch, since it occurs simultaneously with the opening snap. The part of the Y descent between the peak of the V wave and the opening snap notch we have called the opening snap decline.

All left atrial pressure tracings show a lag of 0.02 to 0.03 second. The E.C.G. and phonocardiogram tracings are instantaneous, but the L.A.P. tracings show this lag because of the time taken for

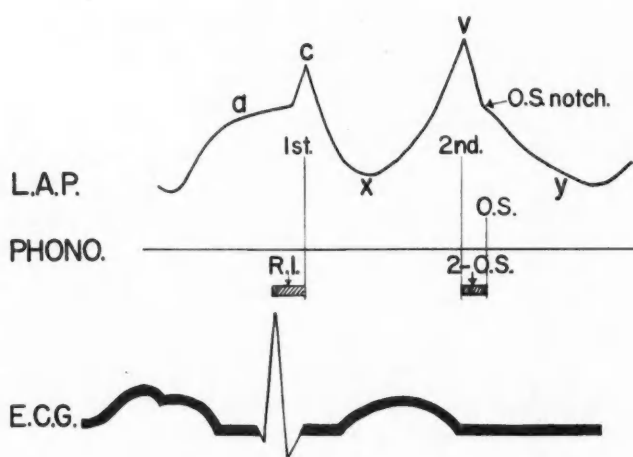


Fig. 1

the pressure wave to reach from the transbronchial puncture to the recording machine. That this lag exists was shown in the early stages of this study. The following method was used. Pressures were taken on the Electronics for Medicine machine with a transducer attached almost immediately to the needle, and simultaneously recorded on a

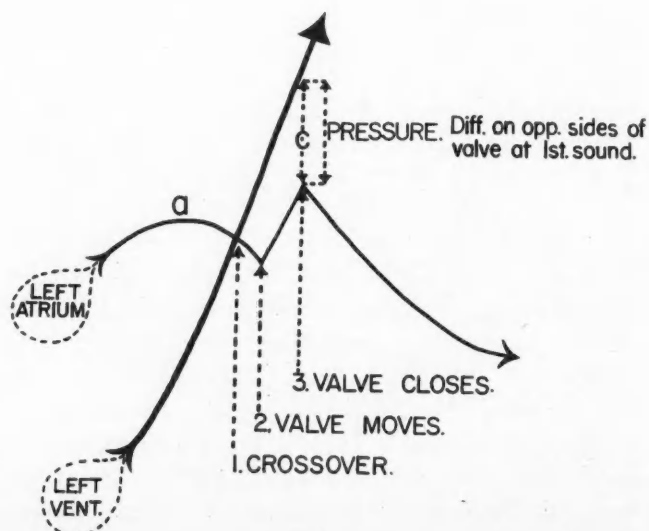


Fig. 2

*Read at the Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Vancouver, January 1959.
†Professor of Clinical Medicine, University of Alberta.

second channel with the catheter, used in the transbronchial puncture, interposed. Scheiner¹ of Electronics for Medicine, Inc., also states: "There is a delay time for the propagation of the pressure wave from the heart to the strain gauge. Such delay times are in the order of 10 to 20 milliseconds, varying with the length of catheter, its size and the material of which it is made."

Moreover, it will be seen from Figs. 8, 9, 10 and 11 that even if no transmission is assumed, the conclusion reached and illustrated by the diagrams (namely that left atrial pressure rises before the opening snap) is not invalidated. Time markings are 0.04 second.* All L.A.P. tracings therefore should be moved to the left about half a mark.

The following observations were made: *The peak of the C wave in the L.A.P. curve corresponds to the maximum vibration of the first sound.* It is therefore produced by the snapping shut of the mitral valve. This is in agreement with the studies of Luisada,² who points out that this wave should be renamed the "av" wave. The old terminology of Mackenzie associates it with transmitted carotid pulsation of the jugular pulse.

The C wave and therefore the first heart sound occur after the crossover of the left atrial and ventricular pressures. In Fig. 2, which shows the left ventricular and the left atrial pressure curves, the possible events which cause this delay are illustrated diagrammatically.

It will be noted that, following the crossover of the curves, there is a lag from interval 1 to 2 before the valve moves. It is assumed that this lag occurs because of the stiffness of the valve. A further build-up of pressure in the left ventricle is necessary after crossover before the valve will move. A second and further delay takes place in the interval 2-3. This represents the time taken for the valve to move down from its deep intraventricular position, where it has been held by the high atrial pressure, to the point of closure in the intra-atrial position.

During the total interval 1-3, there will be a much greater build-up of pressure in the actively contracting ventricle than in the passive atrium. It follows therefore that at point 3, which is the moment of closure of the valve and the time of the first sound, there will be a much higher pressure on the ventricular side of the valve.

This might contribute to the snapping quality of the first sound. It is recognized that another

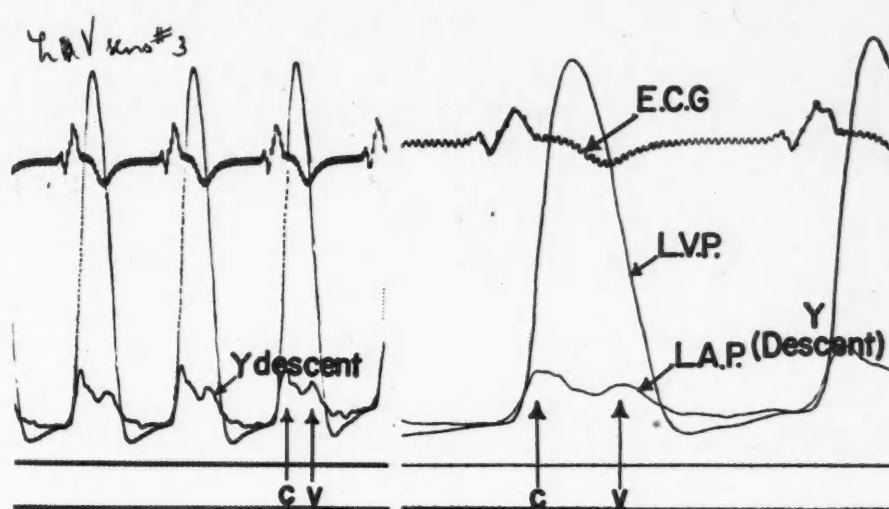


Fig. 3

factor which produces the snapping quality is the following. The normal first sound occurs during the comparatively gentle initial rise of ventricular pressure, whereas the first sound in mitral stenosis will take place near the level of the left atrial pressure (just after the crossover). At this point, the left ventricular pressure is rising steeply. The situation may be analogous to the gentle flapping back of an empty sail from a gentle gust of wind compared with the snapping back from a sudden powerful gust.

In Fig. 3, this point is illustrated on an actual tracing. Pressures in the left atrium and left ventricle were taken simultaneously at operation. It will be seen, especially in the tracing taken at fast speed, that the peak of the C wave occurs after the crossover. The same sequence of events is seen in diagrams published by Braunwald.³ However, this observation was incidental and requires many more pressure tracings before it can be considered proven.

The observation of others that the first heart sound is delayed as measured from the peak of the R wave was only partly confirmed. This is illustrated in Fig. 4, which shows that in 24 cases the R-1 interval was 0.05 second or under, which is within normal range.^{4(c)}

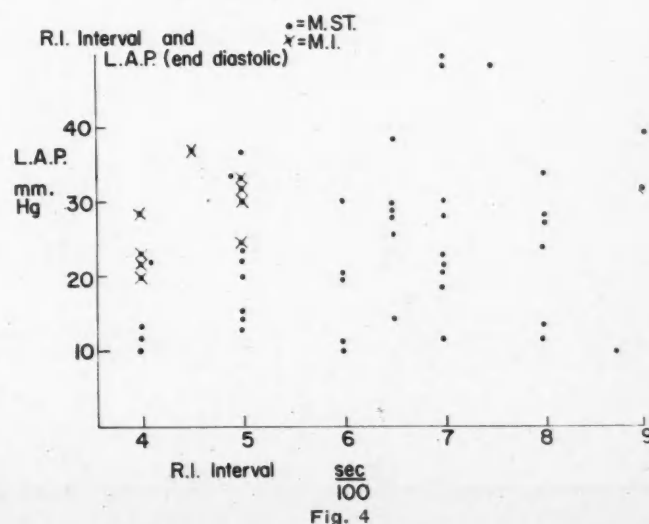


Fig. 4

*Time markings have recorded poorly or not at all on diagrams reproduced here. This should be taken into account in reading them.

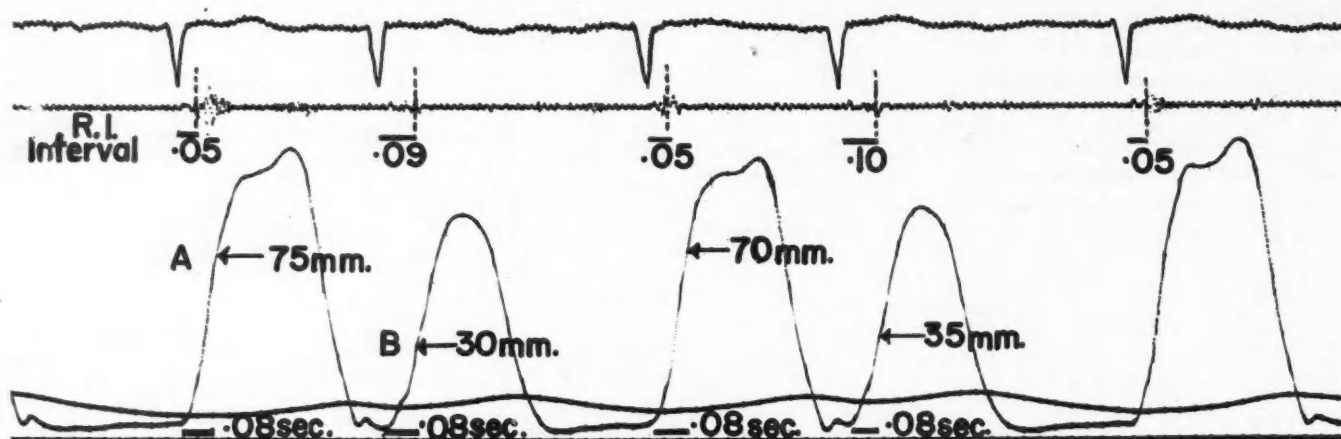


Fig. 5

There was no obvious relation between the delay in the first heart sound and the height of the atrial pressure.⁴ This is also illustrated in Fig. 4, in which the R-I interval is plotted against the left atrial pressure. L.A.P. readings were taken at the peak of C wave.

It has been assumed that the main cause of the delayed sound is related to the height of L.A.P. The atrio-ventricular (A-V) valve cannot snap shut until ventricular pressure equals the raised atrial pressure. If the latter is the only factor involved, the delay should be definitely related to the height of the atrial pressure. Since our study showed no relation, other factors were sought. Stiffness and position of the valve have already been mentioned as factors. The more important factor may be the following.

The delay in the first sound may be related to the filling defect of the left ventricle. As the ob-

struction to the forward flow of blood increases, there will come a time when no further amount of compensatory raising of the pulmonary venous pressure or hypertrophy of the left atrium will compensate for this obstruction. The left ventricle will then fill poorly. A poorly filled ventricle will contract more slowly; it is hypodynamic and may even atrophy and its pressure rise is slow. Conversely, a full ventricle will flap back the valve without much delay.

As an outcome of the conception, the addition of insufficiency to stenosis should shorten the R-I interval. This is in agreement with data reported by Proctor⁶ and is partly confirmed also by Fig. 4. It will be seen that all cases (marked with a cross) where insufficiency is added show a normal R-I interval. The effect of added insufficiency will be further discussed later.

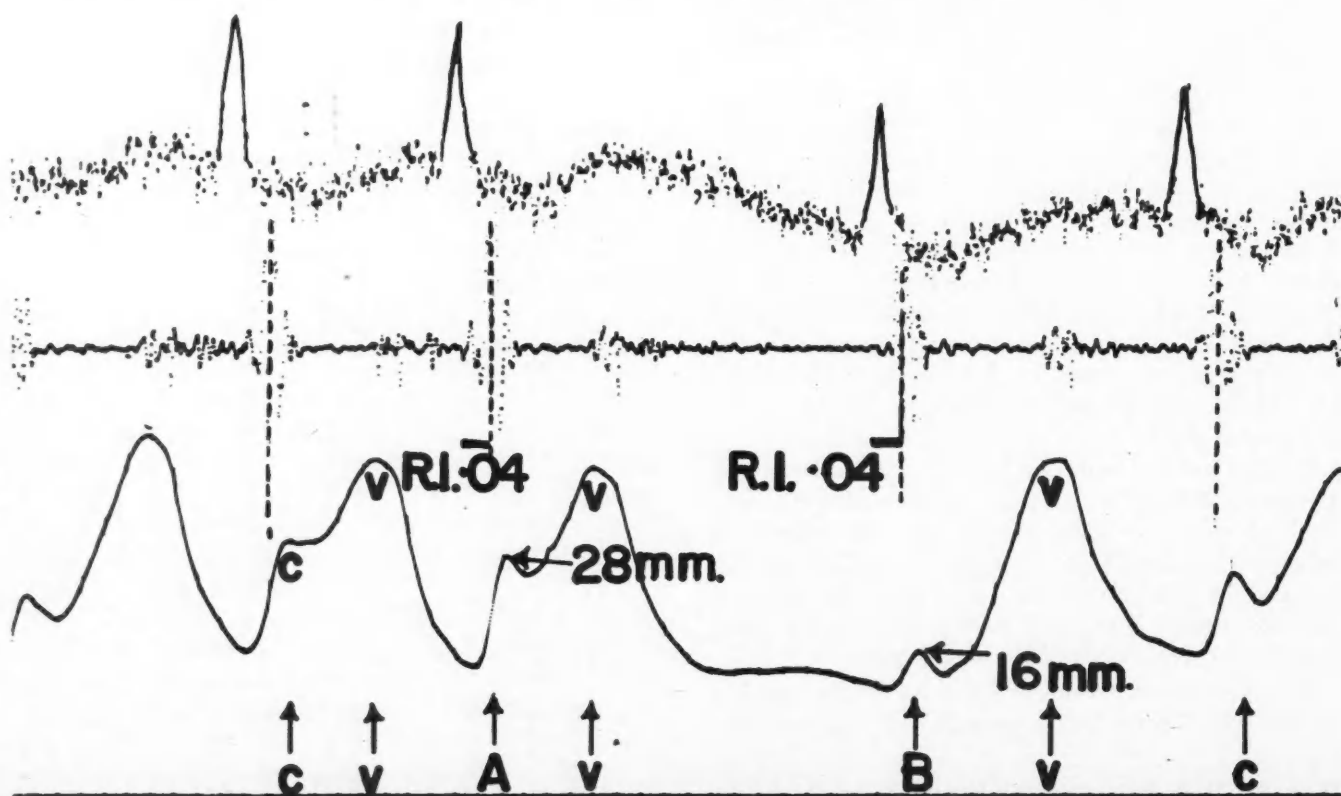


Fig. 6

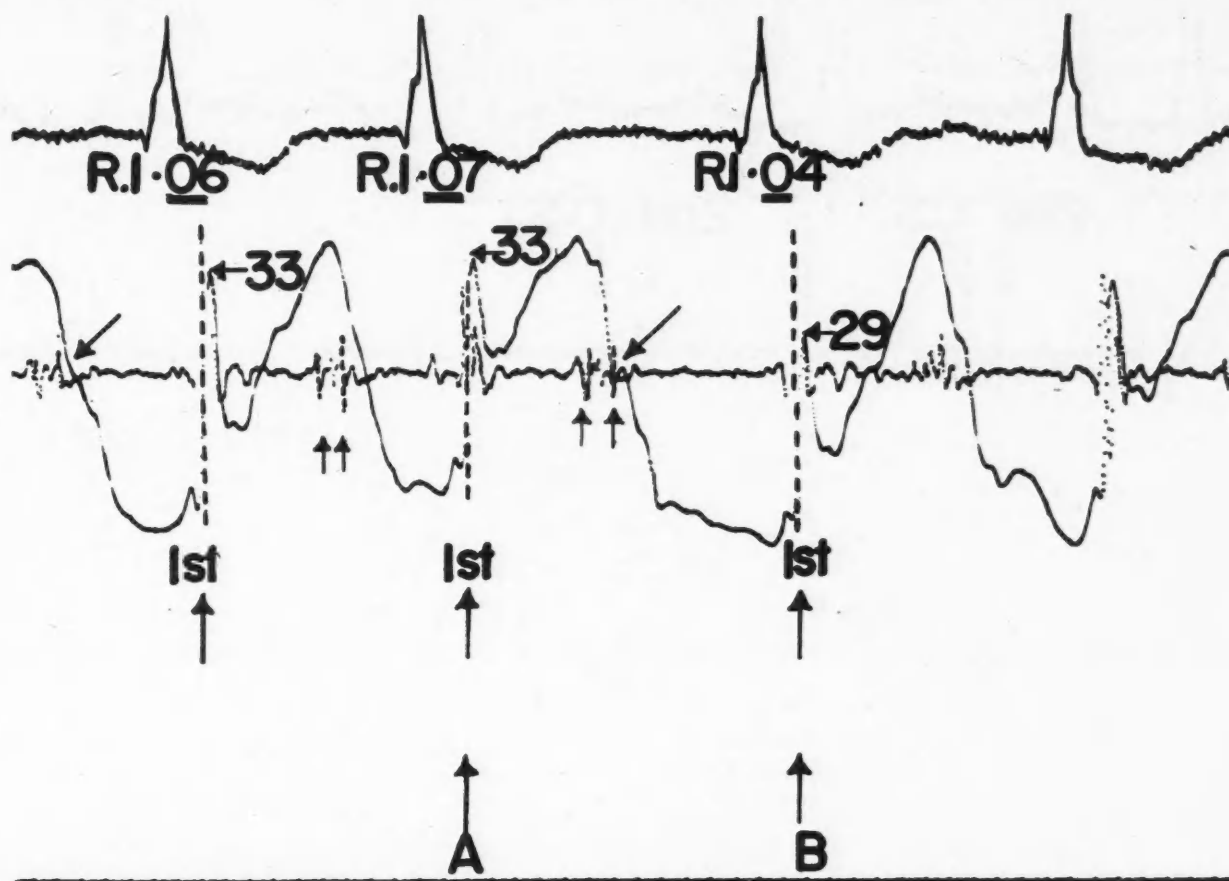


Fig. 7

Further possible confirmation is provided by studying cases of atrial fibrillation and mitral stenosis. In these patients, grossly different degrees of filling of the left ventricle occur.

Fig. 5 shows a tracing of intraventricular pressure taken at operation and combined with a phonocardiograph. Two points are recorded, A and B, both 0.08 second from the onset of ventricular contraction. At point A, the pressure has reached 75 mm. and the R-1 interval is 0.05 second. At point B, the pressure has reached only 30 mm. and the R-1 interval is 0.09 second. Point A has been preceded by a long diastole; the ventricle has filled and it therefore contracts rapidly and pressure rise is also rapid. Point B has been preceded by a short diastole; filling is poor and contraction slow, therefore pressure rise is slow. It is apparent that the delay in the first heart sound would be related here mostly to the rate of pressure rise in the ventricle and not to the actual height of the L.A.P., since even if the L.A.P. remained constant, the gross differences in R-1 interval would be present.

Fig. 6 illustrates this point in reverse. It again shows simultaneous tracings of E.C.G., phonocardiogram and left atrial pressures. This patient had a mixed stenosis and insufficiency. Consequently, the ventricle probably fills even after a short diastole, as at point A. Here it is seen that at A the left atrial pressure is 28 mm. while at B it is 16 mm., yet the R-1 remains constant. The

assumption must be that if the pressure rise in the ventricle is rapid, the difference in the time taken for the ventricle to reach 16 mm. Hg as compared with 28 mm. Hg is too small to be measured. This diagram also illustrates the point that if mitral insufficiency is added to stenosis, the R-1 interval tends to be normal no matter what the height of the left atrial pressure.

Fig. 7 illustrates the point that even with the same left atrial pressure, if ventricular filling is variable, the R-1 interval will vary. At A, the L.A.P. is 33 mm., the R-1 interval is 0.07; at B, the L.A.P. is almost the same at 29 mm., yet R-1 is 0.04. A follows a short diastole; ventricular filling is probably poor and pressure rise is slow, giving a prolonged R-1 interval of 0.07 second. B follows a long diastole; the ventricle has filled and the R-1 interval is normal, 0.04 second, in spite of the same raised L.A.P. In neither case has the length of diastole appreciably altered the L.A.P., probably because the atrio-pulmonary venous reservoir is large and the walls are elastic.

In summary, the delay in the first sound may be mainly dependent on the degree of filling of the left ventricle. However, other factors involved in the delay are the positions of the atrio-ventricular valve at onset of ventricular contraction, and the stiffness of the valve. Another important factor, not previously mentioned, is the electro-mechanical interval.⁷ This will be entirely independent of atrial and ventricular pressures. It is influenced by

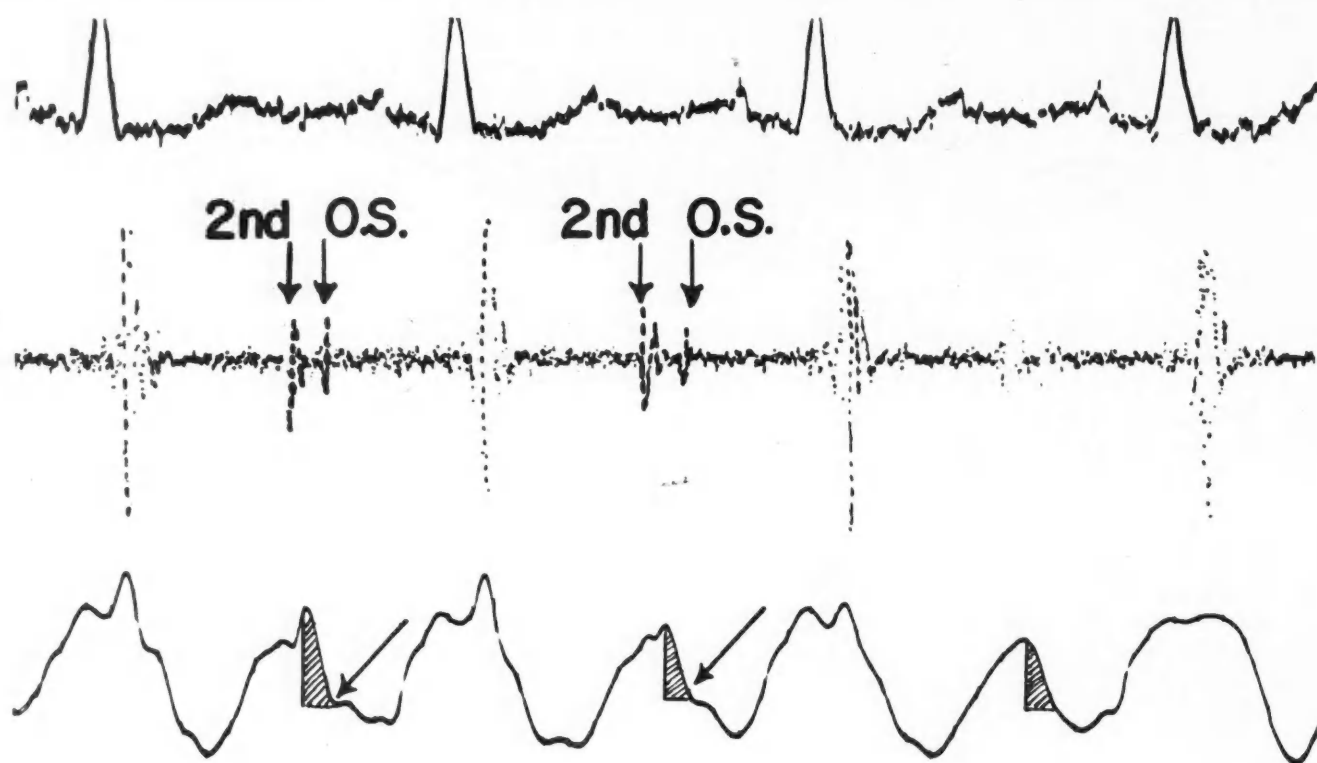


Fig. 8

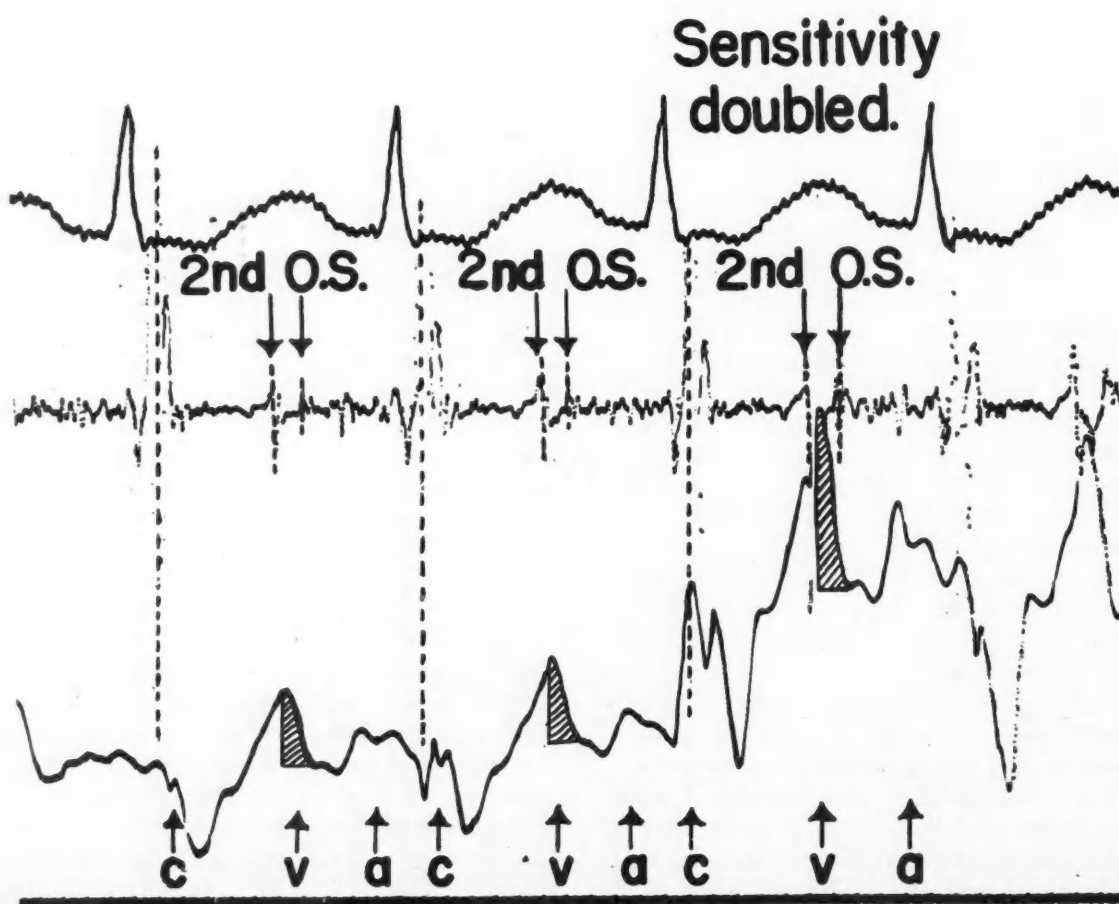


Fig. 9

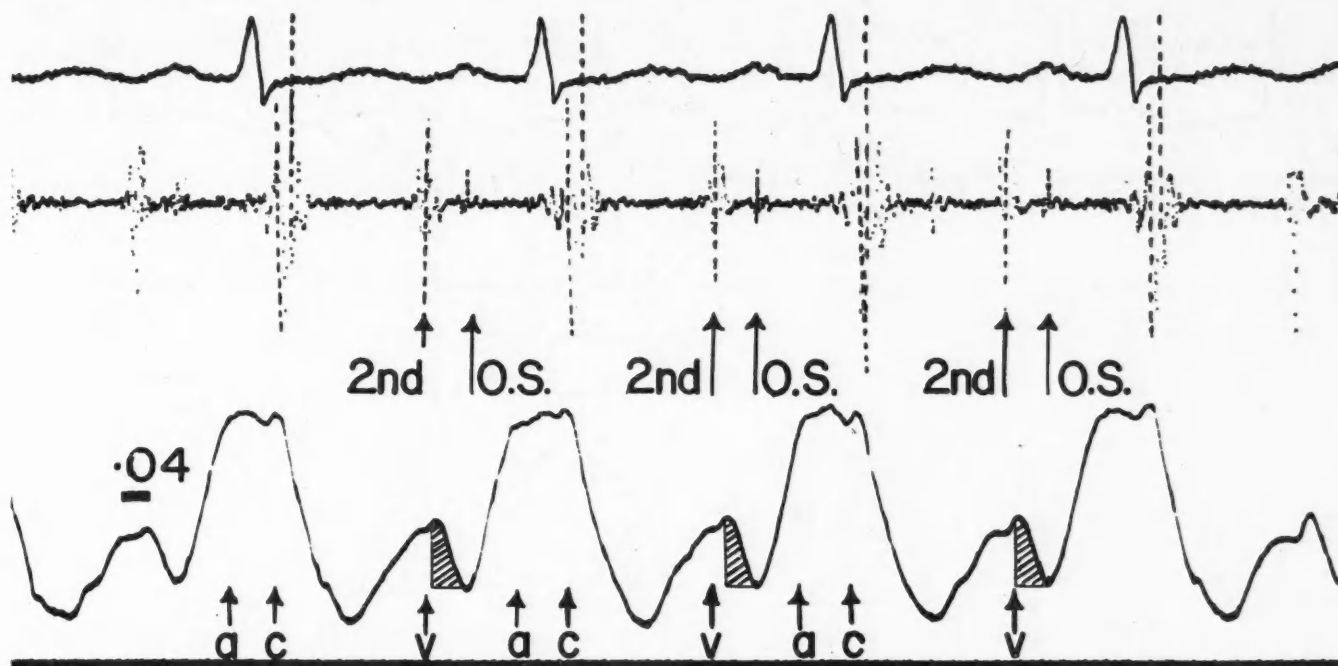


Fig. 10

cardiac rate, height and weight of the individual and other factors not yet studied. Rate of rise of intraventricular pressure will also be influenced by the state of the ventricular muscle (i.e. the presence of coronary disease or cardiac failure),⁹ obstruction to outflow as in aortic stenosis or hypertension, or the presence of extraventricular filling from aortic insufficiency.

The first part of the Y descent on the L.A.P. curve takes place before the opening snap. At the point where the opening snap occurs, a distinct change of angle is seen on the Y descent. This is illustrated in Fig. 8. The first part of the Y descent is shaded and is seen to occur before the opening snap. The change of angle is marked by the arrow. If there is a drop in L.A.P. before the A-V valve opens (at the first part of the Y descent), this drop is unlikely to have anything to do with a flow of blood across this valve. This observation is important and may account for the fact that estimations of the degree of stenosis based on the rate of fall of Y may be quite inaccurate. The fact that after the opening snap there is a change of angle of the pressure curve also points to a different mechanism occurring after the opening snap.

The explanation could be as follows. It is agreed that the movement of the valve, as it snaps shut, is at least partially responsible for the C wave. It is logical to assume that when it snaps open, there will be a corresponding or opposite movement. That is, the first part of the fall of the V wave corresponds to a C wave in reverse. Following this, there is the change of angle which I have called the OS notch, the valve opens and the rest of the Y descent is due to fall of pressure which follows partial emptying of the atrium.

It may be argued that there may be a flow very early in diastole and that the sound called the

opening snap might be delayed until the valve is maximally opened by the high left atrial pressure and a gradient. This seems to the author unlikely for the reasons already given. Even assuming the possibility of this early flow before the OS, it would still seem to be wrong to use this early portion of the V wave as a measure of the amount of stenosis, since it must be influenced also by the movement and mobility of the mitral valve as it travels from the closed to the open position.

Since the first of the Y descent may be due to movement of the A-V valve, this portion may also be an indication of the mobility of the valve. However, all statements on the shape of the L.A.P. curve must be modified, since the shape of this curve must basically be dependent on the volume elastic properties of the veno-atrial reservoir.

Fig. 9 illustrates the same points. Again the part of the Y descent occurring before the OS is shaded. In Fig. 10, the whole of the Y descent is seen to take place before the OS, i.e., all the Y descent takes place before the valve opens and can therefore have nothing to do with the flow of blood across the stenosed valve. Fig. 11 shows the change of angle (arrow) at the OS more distinctly.

The interval between the second sound and the opening snap (2 OS) was compared with the height of the L.A.P. at these points. A better correlation was found than with the R-I interval, but again discrepancies were present. This interval has been the subject of many recent studies^{2, 4(c), 6, 9, 10} and a similar correlation with L.A.P. has been found.⁹

This point is illustrated in Fig. 12, which is a scattergraph showing the L.A.P. (vertical) and the 2 OS interval (horizontal). It will be seen that a fair linear relation is present. The higher the L.A.P., the shorter is the OS interval.

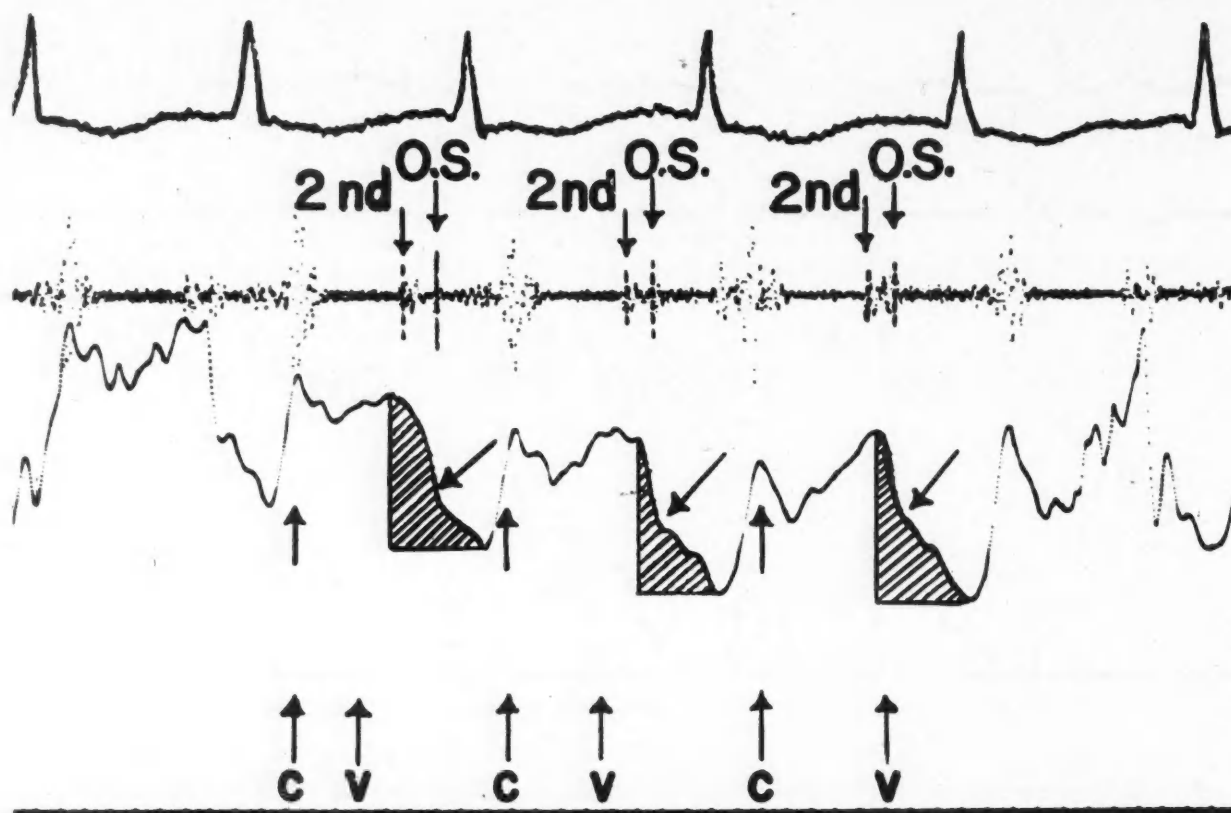


Fig. 11

Although the number of our cases where insufficiency was added to stenosis was small (nine), the following effects of the insufficiency were consistent.

The addition of mitral insufficiency to mitral stenosis shortens the R-1 interval.

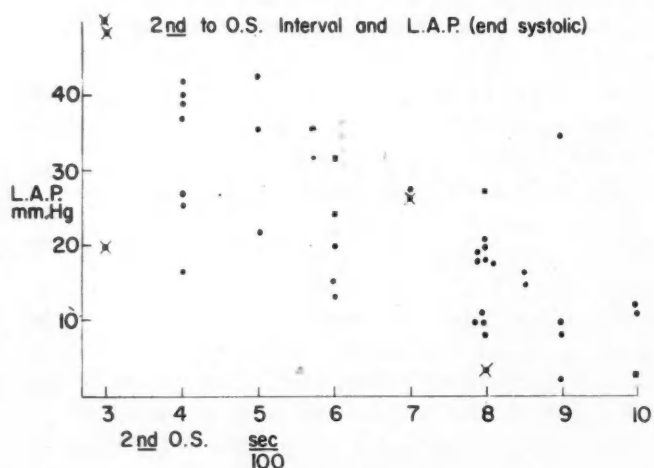


Fig. 12

This observation has already been made, but is elaborated further here. In Fig. 13, it will be seen that in spite of an L.A.P. of 30 mm. Hg at the onset of the first sound, the R-1 interval remains normal (0.04 sec.). In addition to the quick rise of pressure in the well-filled ventricle, which is the main reason for the shortening, other factors may also play a part. The finding of a valve which is insufficient presupposes greater damage, the

valve will be more fibrosed and less mobile, the chordæ tendineæ shortened. Less time will therefore be spent in travelling from the closed to the open position. Insufficiency will also mean less obstruction; the atrial pressure will therefore have fallen during diastole. At the onset of the first sound, it may be relatively low in spite of a high mean. Less time is then necessary for the intra-ventricular pressure to reach intra-atrial pressure and for it to close the valve.

The addition of mitral insufficiency shortens the 2 OS interval or causes the opening snap to disappear.

Of the nine cases of mixed stenosis and insufficiency, three had a 2 OS interval of less than 0.04 second; in the remainder it was absent.

This may be explained as follows. In mitral insufficiency a greater stretch occurs. This will mean (Starling's Law) a more rapid rise in intra-ventricular pressure. It is likely that a quick rise would mean a quick fall, thus shortening the interval. The onset of the second will also depend on events entirely outside left intra-atrial or intra-ventricular pressures. These factors might be the state of the aortic valve, the size and elasticity of the aortic reservoir and the peripheral resistance. Since this is so, no very accurate relation between L.A.P. and the 2 OS can be expected. The decreased mobility of the A-V valve will also tend to shorten this interval as it does the R-1 interval. As with the R-1 interval, although in reverse, pressures in the left atrium will rise in systole in proportion to the leak. They may therefore be very high in relation to the mean L.A.P. at the end of systole.

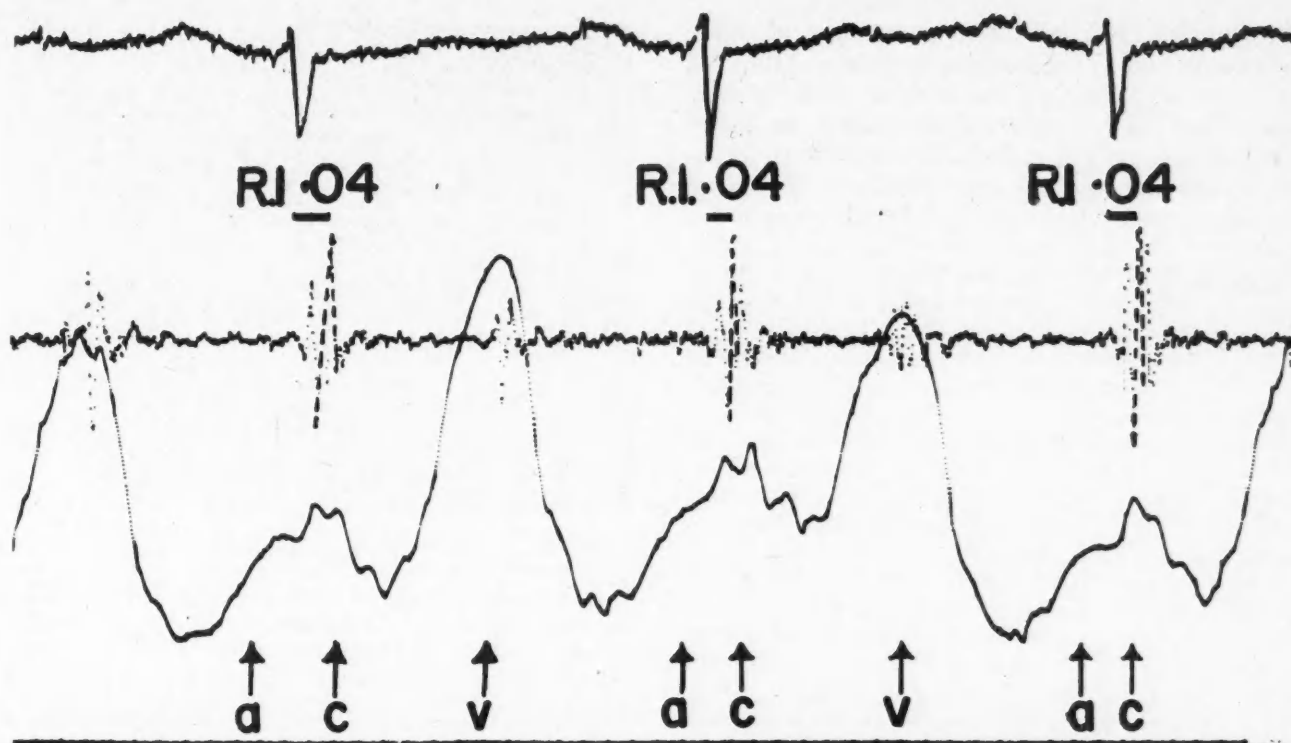


Fig. 13

Consequently, the pressure at the time of the second sound may be nearly the same as the L.A.P., thus shortening or obliterating the 2 OS interval. Finally, a valve which is almost immobile may be incapable of snapping shut.

When insufficiency is added to stenosis, the V wave is high and its descent may start even before the second sound.

This is illustrated in Fig. 14. This is a second reason why the first part of Y descent may have nothing to do with the degree of stenosis, since it is certain that at this time the A-V valve is not open.

It is probable that the explanation of this early fall is different from that given in pure stenosis and is as follows. With the addition of incompetence, the late rise of pressure in the atrium (the V wave) is due partly to retrograde flow of blood from ventricle to atrium. This wave of insufficiency may be separate from or added to the V wave and is named the I wave by Luisada. This is why the V wave may be so tall, i.e. the V wave is really a V-I wave since the separation is probably difficult to see in most cases. As systole nears its end, this reflux diminishes and stops. This will contribute to the cessation of rise and perhaps the early fall. Most of the early

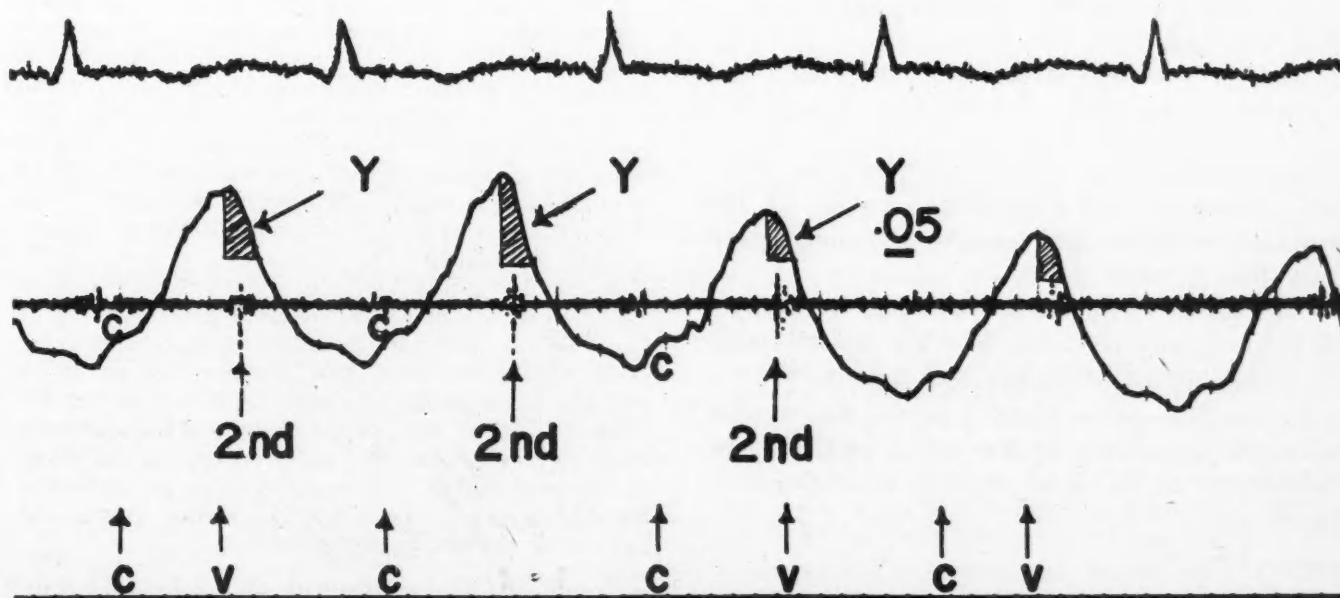


Fig. 14

fall, however, will be due to the reflux of blood backwards into the pulmonary veins. After all, there are no valves at the atrio-venous junction. This effect is the same as the reflux of blood which occurs on the right side with tricuspid insufficiency and produces a systolic pulsation of the jugular veins and liver.

SUMMARY

The peak of the C wave in the left atrial pressure (L.A.P.) curve seems to correspond with the closing snap of the mitral valve. This peak, in the few cases studied, occurred after the crossover of left atrial and ventricular pressure curves. The first heart sound is not always delayed in mitral stenosis. The delay, when it occurs, may be related mainly to the degree of filling of the left ventricle. Position and degree of mobility of the valve also influence this delay.

The first heart sound is apparently not delayed, if significant insufficiency is added to stenosis.

The first part of the Y descent in the L.A.P. curve, in both pure mitral stenosis and mixed stenosis with insufficiency, takes place before the opening of the A-V valve. Estimations of the degree of stenosis, made by measuring the rate of Y decline, may therefore be inaccurate.

Phonocardiography may therefore be an aid in establishing the diagnosis and degree of severity of mitral stenosis. It may also help in differentiating it from insufficiency and in estimating the degree of filling of the left ventricle.

I am deeply grateful to Dr. A. A. Luisada for his interest and comments. This study was made possible by the help of my colleagues, Drs. Robert Fraser, J. Dvorkin, Gordon Bell, J. C. Callaghan, R. E. Rossill, Colin Ross and Colin Dafoe.

TRAUMATIC ARTERIAL LESIONS AND CEREBRAL THROMBOSIS*

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TRAUMATIC lesions of arteries supplying brain tissue are of interest and importance because of the vascular occlusion and cerebral softening which they may produce.

The vessel wall may be damaged by indirect or by direct violence and the lesions may therefore be a complication of head or neck injuries.

Of the nine cases reported below, the number in which the trauma to the vessel wall must be considered to be due to indirect violence is significant.

*From the Division of Neuropathology, University of Toronto. Delivered (E.A.L.) before the Ontario Association of Pathologists, October 1957.

REFERENCES

1. SCHEINER, M.: Personal communication.
2. LUISADA, A. A. AND LIU, C. K.: Cardiac pressures and pulses, Grune & Stratton, Inc., New York, 1956.
3. BRAUNWALD, E. et al.: *Circulation*, 12: 69, 1955.
4. WELLS, B. G., RAPPAPORT, M. B. AND SPRAGUE, H. B.: *Am. Heart J.*, 37: 586, 1949.
WELLS, B.: *Brit. Heart J.*, 16: 261, 1954.
CRAIGIE, E.: *New England J. M.*, 257: 650, 1957.
POTVIN, R. AND STUBINGTON, D.: *Canad. M. A. J.*, 77: 1015, 1957.
5. KELLY, J. J., JR.: *Am. J. Med.*, 19: 862, 1955.
6. PROCTOR, M. H. et al.: *Am. J. Med.*, 24: 861, 1958.
7. STROBER, M., MARTINEZ, F. AND KELLY, J. J., JR.: *Am. Heart J.*, 54: 684, 1957.
8. WOOD, P. H.: Diseases of the heart and circulation, 2nd ed., Eyre & Spottiswoode, Ltd., London, 1956.
9. BAYER, O., LOOGEN, F. AND WOLTER, H. H.: *Am. Heart J.*, 51: 234, 1956.
10. HAUCH, H. J.: *Klin. Wchnschr.*, 34: 189, 1956.

RÉSUMÉ

Le sommet de l'onde C semble correspondre au claquement de fermeture de la valvule mitrale. Ce sommet dans les quelques cas étudiés se situa après le point de croisement des courbes de pression de l'oreillette et du ventricule gauches. Le premier bruit n'est pas toujours retardé dans cette lésion; lorsqu'il y a retard on peut le rattacher au degré de remplissage du ventricule gauche. La position et la mobilité de la valvule peuvent aussi modifier ce retard. Le premier bruit ne semble pas retardé si une insuffisance importante accompagne la sténose. La première phase de la descente y dans la sténose mitrale pure et dans celle qu'accompagne l'insuffisance se produit avant l'ouverture de la valvule auriculo-ventriculaire. L'évaluation de la sténose si elle est fondée sur le degré de pente de la descente y risque donc de souffrir d'imprécision. La phonocardiographie peut contribuer à établir le diagnostic et la sévérité de la sténose mitrale; elle peut aussi aider à différencier l'insuffisance et à déterminer l'état de remplissage du ventricule gauche.

HEAD INJURIES

CASE 1.—A.V. (NP: 389-43), a woman of 25 years, was murdered by multiple hammer blows to the vault of the skull. Post-mortem examination showed multiple compound comminuted fractures of the vault of the skull, mainly in the temporal and occipital regions. The fractures extended into the left middle and both posterior cranial fossæ. The left occipital lobe was almost completely separated from the rest of the brain. A piece of bone had been forced into the left frontal lobe to a depth of 1½ inches (3.75 cm.).

A routine section of the right middle cerebral artery (Fig. 1) shows the internal elastic lamina of the vessel to have been detached from the underlying media and to be curled up in the vessel lumen. Fresh red blood corpuscles are seen on both sides of the detached lamina. The amount of internal elastic lamina tissue is greater than that required to line the vessel at the level of this section. It is therefore presumed that the lamina has been ruptured by the trauma and has recoiled from the site of rupture.

Comment.—The mechanism of the indirect traumatic vascular lesion in this devastating head



Fig. 1.—Low power view ($\times 90$) of right middle cerebral artery of Case 1, stained with H&E. This shows very recent severe traumatic rupture and dislocation of the internal elastic lamina.

injury may have been stretching or twisting of the vessel wall or, possibly, vibration of the vessel caused by repeated hammer blows.

CASE 2.—E.B. (NP: 406-43), aged 58, was said to have been drinking and to have fallen during a "playful scuffle". He was thought to have hit his head in his fall but was fully conscious until he became drowsy one hour later. As he could not be roused, he was admitted to hospital within a few hours of his fall.

On admission, he was unconscious with complete flaccid right hemiplegia. There were no external signs of injury, and x-ray examination was negative for fracture of the skull. His blood pressure was normal. Lumbar puncture withdrew clear fluid under a pressure of 220-250 mm. H_2O . Bilateral operative burr holes revealed no sign of extradural and subdural haemorrhage. His respirations became stertorous and Cheyne-Stokes in type shortly before he died, two days after his fall.

Post-mortem examination showed acute bronchopneumonia of the right lung. His brain weighed 1545 grams. There was recent softening, compatible with two days' duration, in the complete distribution

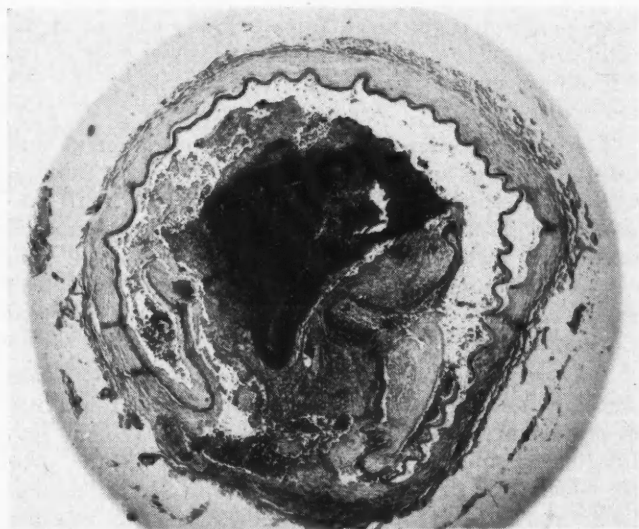


Fig. 2.—Recent traumatic haemorrhage into wall of left middle cerebral artery of Case 2. This shows rupture of the internal elastic lamina with extension of thrombus into the severely narrowed vessel lumen.

of the left middle cerebral artery. He had increased intracranial-pressure haemorrhage in the midline pontine tissues.

The left internal carotid and the proximal 5.0 mm. of its middle cerebral branch were distended with recent thrombus occluding their lumina.

Microscopical examination of these vessels showed (Figs. 2 and 3) what was considered to be a primary massive haemorrhage into the medial coats of the vessels, displacing the intima inwards. The internal elastic lamina was ruptured at the apex of this intramural haemorrhage, allowing extension of recent thrombus into the severely narrowed vessel lumen (Fig. 2). The haemorrhage had occurred under a localized plaque of arteriosclerotic thickening of the intima (Fig. 3).

Comment.—This complication of a slight head injury was interpreted as being due to indirect traumatic bruising of the walls of the left internal carotid and middle cerebral arteries against adjacent bony structures, e.g. the left anterior clinoid

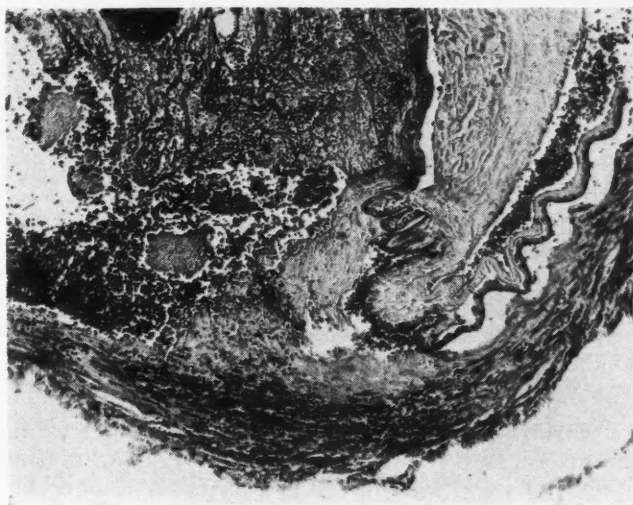


Fig. 3.—Higher power view of edge of lesion shown in Fig. 2. The haemorrhage has elevated a small arteriosclerotic plaque into the vessel lumen, which is seen to the right of the photograph.

process. The subsequent thrombotic occlusion of these vessels could therefore be considered as a direct result of this man's slight head injury.

A similar sequence of events is not uncommon in Workmen's Compensation problems.

Direct trauma to intracranial arteries can of course be caused by penetrating injuries. The following case is an example.

CASE 3.—A.W. (NP: 399-49), aged 34 was murdered by a single bullet wound which entered his face below his left eye. The bullet track entered the brain at the inner end of the stem of the left lateral fissure, severely damaging the main trunk of the left middle cerebral artery. The left internal carotid artery proximal to this damaged vessel was intact. Its lumen contained firm blood clot which microscopically showed very early platelet thrombus.

Of more interest and importance are the following two cases in which manipulation of intra-

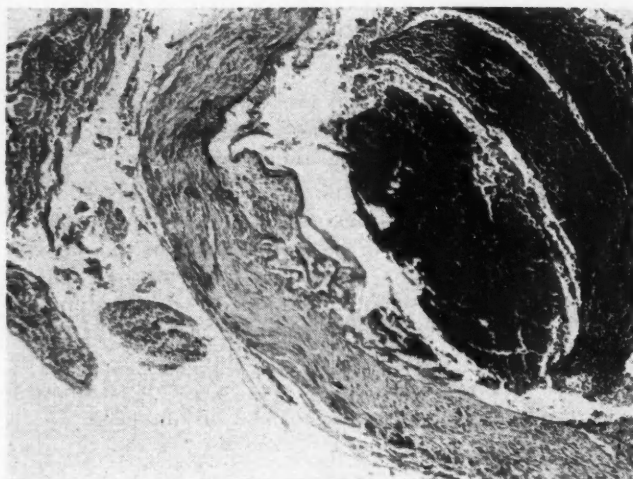


Fig. 4.—Left internal carotid artery of Case 4. This shows localized traumatic rupture of the internal elastic lamina, with hæmorrhage under the displaced lamina and adhesion of early thrombus to the exposed medial coat.

cranial arteries during operation has probably been responsible for thrombosis in their lumina.

CASE 4.—W.C. (NP: 112-50), a 68-year-old man, died on the day after an unsuccessful direct surgical attack on a large aneurysm in the neighbourhood of the left internal carotid artery. During the operation this vessel had to be ligatured in the neck to control massive hæmorrhage from the intracranial aneurysm.

At post-mortem examination the left internal carotid and middle cerebral arteries contained recent thrombus. Microscopically a transverse section through the left internal carotid artery showed a rupture of the internal elastic lamina (Fig. 4), with recent thrombus attached to the exposed area of the medial coat.

Comment.—The rupture of the internal elastic lamina of this vessel is believed to be due to the operative manipulation of the adjacent aneurysm. The thrombosis was of course facilitated by the ligation of the vessel in the neck on the day before the patient died.

CASE 5.—M.S. (NP: 350-45), at the age of 53, underwent her third operation for removal of a large, recurrent chromophobe adenoma of the pituitary gland. She was conscious after the closure of the dura, but as the scalp was being closed she had a chill, her pulse slowed to 60 and she could not perform voluntary movements of her right arm. She became unconscious and died 16 hours after operation.

Post-mortem examination: A dissection of the left internal carotid artery showed it to be closely adherent to the capsule of the pituitary tumour. Very recent softening in the cortical distribution of the left middle cerebral artery was confirmed microscopically.

A transverse section of the left internal carotid artery, at the site of its adhesion to the tumour capsule, shows microscopically that the lumen contains platelet thrombus. The wall (Fig. 5) shows a localized rupture of the internal elastic lamina under an arteriosclerotic plaque. Red blood corpuscles have passed through this rupture into the subintimal and medial coats of the vessel. There is early reaction by polymorphonuclear leukocytes to this hæmorrhage into the vessel wall.

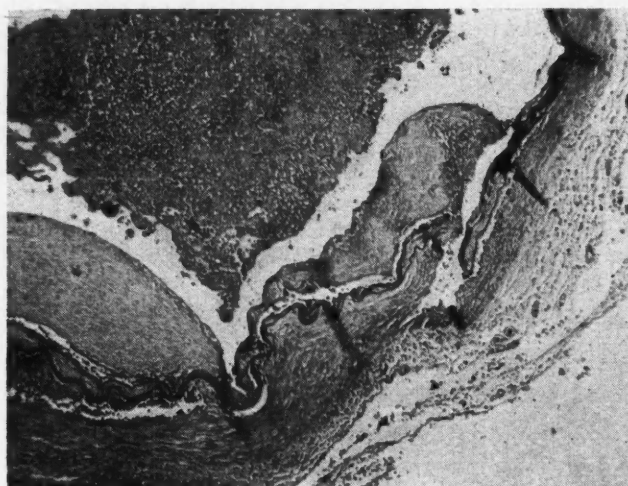


Fig. 5.—Case 5, showing similar localized traumatic rupture of the internal elastic lamina of the left internal carotid artery. The wall of this vessel shows considerable arteriosclerosis. Recent thrombus is seen in its lumen. (H. & E., $\times 72$.)

Comment.—In this case there appears to be a clear relation between the surgical manipulation of this woman's tumour and the rupture of the internal elastic lamina of her left internal carotid artery, which led rapidly to platelet thrombosis in the lumen of the vessel. It is of great interest that the origin of her right hemiplegia was noted by the surgeon immediately after the end of the operation.

NECK INJURIES

The following four cases illustrate the effects of trauma to the internal carotid artery in the neck.

CASE 6.—F. (NP: 445-45), a German prisoner-of-war, died 28 hours after sustaining a rifle gunshot wound in the upper part of his neck. He vomited large quantities of blood 1½ hours after being wounded and was unconscious an hour later. Semiconsciousness was restored with plasma, but he developed respiratory difficulties and his blood pressure fell to 85/50 mm. Hg. On admission to hospital 11 hours after wounding, a through-and-through gunshot wound was found to have penetrated the neck from below and behind the right angle of the jaw, fracturing the lower part of the left ramus of the mandible. There was a flaccid left hemiplegia.

Post-mortem examination: The right common and external carotid arteries were patent. The right internal carotid artery showed discoloration of its wall immediately distal to the bifurcation. Its lumen contained occluding thrombus for a distance of 1.5-2.0 cm. above the bifurcation of the vessel. The brain showed early softening in the region of the right internal capsule.

Microscopically a longitudinal section of this vessel showed the lumen to contain recent platelet thrombus, firmly adherent to the intima. The intimal coat was irregularly thickened and had ruptured in the area to which the thrombus was adherent. A little fresh hæmorrhage was found at the base of this rupture. The medial coat of the vessel was intact. Hæmorrhage, with reacting polymorphonuclear leukocytes, was found in the adventitial coat.

Comment.—This man's traumatic internal carotid thrombosis would appear therefore to have been due to severe bruising of the vessel wall which had caused intramural hæmorrhage into the adventitia and localized rupture of the internal elastic lamina.

CASE 7.—B. (NP: 444-45) a German prisoner-of-war, lived for three days after receiving a rifle gunshot-wound in his upper neck, similar in level to that of Case 6. On admission to hospital on the day after his wounding, the bullet track was found to extend from an entry wound $3\frac{1}{2}$ inches (8.75 cm.) directly behind the left angle of the lower jaw to its exit wound on the right side of the upper part of the nose. Neurological examination showed him to be conscious but drowsy. There was nominal aphasia. Palatal movement was depressed on the left and the tongue deviated to the left. The right arm was flaccid, the right leg spastic. He had hemianæsthesia on the right with loss of position sense. He died in respiratory distress in spite of an emergency tracheotomy performed on the day before his death.

Post-mortem examination: The left internal carotid artery had a defect in its wall $\frac{1}{2}$ inch (1.25 cm.) in length. The upper end of this defect was $\frac{1}{2}$ inch below the foramen lacerum medium. The adjacent left vagus nerve was bruised and torn.

The specimen received for microscopical examination confirmed thrombosis of the upper part of the left internal carotid artery for a length of 2.5 cm. The traumatic rupture of the vessel wall was seen at the top of the specimen. Platelet thrombus filled the mouth of the defect and the lumen of the vessel below the defect. The sections of the left vagus nerve included its trunk ganglion, the nerve cells of which showed acute degenerative changes. Traumatic hæmorrhage was seen in the bundles of nerve fibres.

Comment.—This therefore is an example of direct traumatic laceration of the internal carotid artery by a rifle bullet wound of the neck. It is of interest that no significant hæmorrhage could have occurred from the ruptured vessel, as the patient lived for three days. It is also, perhaps, of passing interest that this healthy young soldier with, presumably, a normal circle of Willis should have suffered a complete right hemiplegia as a result of rupture and thrombosis of the left internal carotid artery in his neck.

CASE 8.—T. (NP: 443-45), a German prisoner-of-war, lived for two days after having been wounded in the neck by a high explosive bullet. He was found to have a spastic left hemiplegia on admission to hospital, and the diagnosis of a lesion of the right internal carotid artery was made.

Surgical exploration of the right side of the neck on the day before his death showed the right internal jugular vein to be torn, and this vessel was ligatured. The wall of the adjacent right internal carotid artery was bruised and was thought to be in spasm. A metallic foreign body at the level of the third cervical vertebra was removed. The patient's postoperative course was satisfactory for 10 hours. He died of gradually increasing respiratory failure. His heart con-

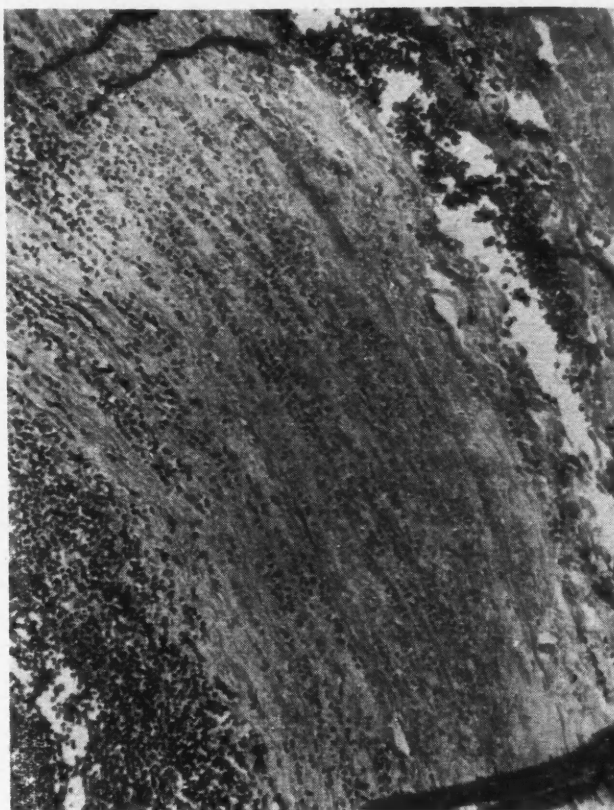


Fig. 6.—Wall of right internal carotid of Case 8. The structures of the wall are partially necrotic and are severely infiltrated by red blood corpuscles and polymorphonuclear leukocytes. Hæmorrhage is seen into the adventitia to the right of the photograph. The early thrombus in the vessel lumen is seen in the lower left corner. ($\times 180$.)

tinued to beat for 20 minutes after his respirations ceased.

Post-mortem examination showed a thrombus in the right internal carotid artery. There was no damage to the high cervical spinal cord. Early softening was found in the distribution of the right internal carotid artery.

Portions of the right internal and external carotid arteries were received for microscopical examination. The external carotid showed a uniform slight thickening of its intima but it was otherwise normal. The lumen of the internal carotid was greatly distended by recent thrombus. The wall of the vessel was partially necrotic and heavily infiltrated by red blood corpuscles and polymorphonuclear leukocytes. In places this infiltration was so severe that the normal components of the vessel wall could not be identified (Fig. 6).

Comment.—Here again, the mechanism of this traumatic thrombosis would appear to be indirect violence. It is likely that the metallic foreign body found at operation passed close to the vessel, as it ruptured the right internal jugular vein. The partial necrosis of the vessel wall was apparently due to diffuse hæmorrhage into all the vessel coats. Destruction of the media is probably responsible for the extreme distension of the vessel lumen found at post-mortem examination. This appears to have been preceded by spasm, noted by the surgeon at operation on the day before death.

It is tempting to wonder whether the passage of this high explosive shell fragment could have caused vibration of the vessel to produce these lesions in its wall.

CASE 9.—G.M. (NP 4753), 53-year-old, was found lying on the lawn of his house in a stuporous state and partially paralyzed on the right side. On admission to hospital, there was a little dried blood on the skin of the neck on the left side extending up to behind the left ear. There was a visible swelling of the soft tissues around the left angle of the mandible. A small puncture wound of the skin overlay this soft tissue swelling.

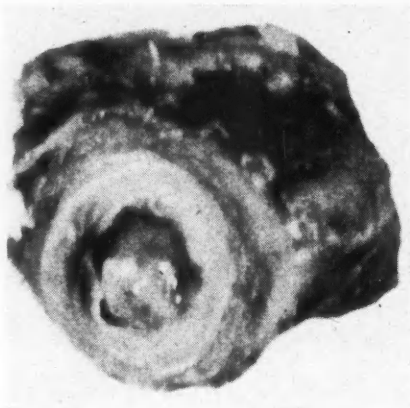


Fig. 7.—Gross specimen of left internal carotid artery of Case 9. The lumen contains recent thrombus. The wall is thickened and oedematous. Hæmorrhage is seen in the adventitia.

Arteriography showed complete occlusion of the left internal carotid artery about 1 inch (2.5 cm.) above the carotid bifurcation, and operation was performed under hypothermia. The puncture wound track was traced inwards and was found to end within the lumen of the ruptured left internal carotid artery. The rupture was $\frac{1}{4}$ – $\frac{1}{2}$ inch below the base of the skull and could not be repaired. The artery was ligatured above and below the rupture, portions of the intervening part of the vessel being sent for histological examination. The operative specimen received (Fig. 7) showed thrombosis with oedematous swelling of the vessel wall and hæmorrhage in the adventitial coat.

Microscopically, the lumen of the vessel contained recent thrombus (Fig. 8). The intima showed early endothelial proliferation with adhesion to the thrombus. The subintimal tissue was uniformly thickened in conformity with the patient's age. The muscle fibres of the media were separated by oedema. The adventitia was markedly thickened by hæmorrhage, oedema, increased vascularity and early fibroblast reaction (Fig. 9).

Comment.—The main interest of this case of direct traumatic laceration of the wall of the internal carotid artery is the insignificant size of the puncture wound which produced it. Until operation was performed the tiny wound in the skin was considered to be a superficial laceration.

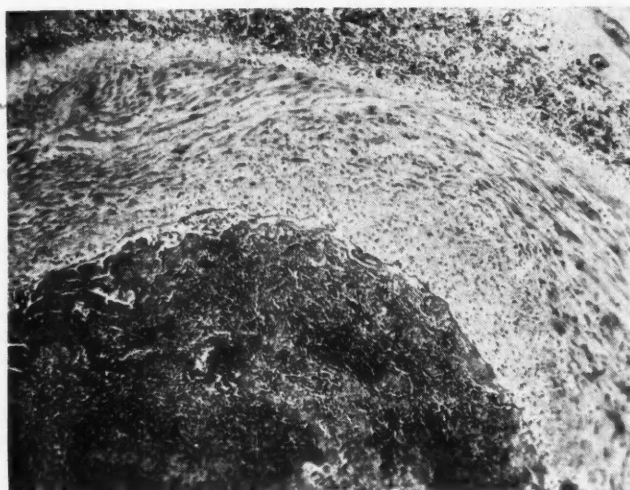


Fig. 8.—Low power view, $\times 72$, of vessel wall of Case 9. The lumen contains recent thrombus. The subintimal coat is thickened. The oedema of the media and the hæmorrhage in the adventitia are seen in the upper part of the photograph.

GENERAL COMMENT

A study of these cases shows the vulnerability of the internal carotid and middle cerebral arteries not only to direct but also to indirect violence. The intima is the coat most uniformly damaged, and rupture, with recoil, of the internal elastic lamina appears to be responsible for the deposition of thrombus, probably on the medial coat where it has lost its intimal covering. Recoil of the elastic tissue in the walls of small arteries has been postulated for generations as one of the effective agents in the stoppage of hæmorrhage from such small vessels which have to be cut in surgical operations.

Artefacts, either from stretching of the vessel at post-mortem examination or in the preparation of the microscopical sections, can be eliminated as a cause of the damage to the internal elastic lamina in the cases described above, because, except in Case 1 in which death was probably almost immediate, reactive changes can be seen microscopically in the damaged wall.

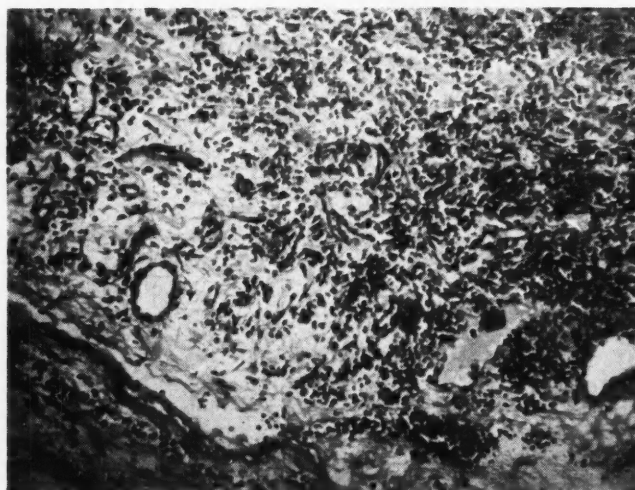


Fig. 9.—Higher power view, $\times 216$, of adventitia of the left internal carotid artery of Case 9. There is oedema and early fibroblast reaction to the hæmorrhage.

A case of arterial thrombosis in which trauma could possibly have played a part therefore merits careful pathological examination of the vessel involved, both grossly and microscopically. This is particularly important in cases, such as Case 2, where hemiplegia had occurred following a slight head injury.

Our thanks are due to the staff of the Toronto General and Western Hospitals, to Dr. Smirle Lawson, Supervising Coroner for the Province of Ontario and to Dr. Cameron Gray for the war material.

LES STAPHYLOCOCCIES BULLEUSES: URGENCES RESPIRATOIRES

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INTRODUCTION

ON SEMBLE d'accord aujourd'hui sur l'étiologie staphylococcique d'une maladie bulleuse du nourrisson. On semble aussi d'accord sur le traitement médical de l'aspect infectieux de ce problème. Les opinions sont partagées cependant sur la conduite à tenir en face des manifestations mécaniques de la maladie. Tout dernièrement, le pendule a semblé osciller vers un conservatisme inquiétant. La présente étude de nos cas à l'Hôtel-Dieu St-Vallier a été entreprise dans le but d'évaluer nos résultats et de jeter un peu de lumière sur les contributions de la chirurgie dans les états d'urgence qui accompagnent le gonflement d'une bulle.

Méthode et matériel.—Tous les cas de staphylococcie bulleuse diagnostiqués et traités dans notre institution ont été revus. La présence de bulles a été prouvée radiologiquement. La présence de staphylocoques a été prouvée dans tous les cas, sauf un, par culture de liquide retiré à la ponction (Tableau I). Le plus jeune patient avait deux mois et le plus vieux, quatre ans. L'âge moyen dans cette série était de neuf mois. A noter aussi la prépondérance nette des bébés mâles sur les bébés de sexe féminin, la proportion étant dix contre trois.

Symptômes chirurgicaux.—S'ajoutant aux symptômes infectieux d'origine microbienne, des symptômes d'ordre mécanique nécessitant une intervention chirurgicale sont survenus chez sept de nos patients, soit une fréquence de 55%.

Le gonflement soudain d'une bulle staphylococcique s'accompagne de dyspnée intense et de

RÉSUMÉ

Ce travail illustre la vulnérabilité de la carotide interne et de la cérébrale moyenne aux traumatismes non seulement directs mais aussi indirects. La tunique interne est la plus souvent endommagée; la rupture de la couche élastique interne par contraction semble responsable de la déposition de thrombus probablement sur la tunique moyenne où l'intima a été détruite. On a considéré pendant des générations que la contraction du tissu élastique dans la paroi des petites artères était un des agents efficaces de l'hémostase quand ces vaisseaux sont coupés au cours d'une opération. Les thromboses artérielles survenant à la suite de traumatismes méritent que l'on consacre un examen anatomo-pathologique minutieux aux vaisseaux impliqués. Un tel examen s'impose dans les cas d'hémiplégie provoquée par une blessure crânienne banale comme il arriva à l'un des neuf malades dont les données cliniques et histologiques sont fournies dans le texte.

TABLEAU I.

Cas	Sexe	Age	Traitement	Hospitalisation
1	M.	5 mois	Médical	32 jours
2	M.	27 jours	Médical	22 jours
3	M.	4 ans	Médical	60 jours
4	M.	9 mois	Drainage fermé (3) Ponction pleurale (2) Ponction du péricarde Péricardiectomie	42 jours
5	M.	4 mois	Médical	9 jours
6	F.	3 mois	Médical	31 jours
7	M.	5 mois	Drainage fermé (2) Thoracentèses (5)	35 jours
8	M.	3 mois	Drainage fermé (4) Thoracentèses (2)	66 jours
9	F.	6 mois	Drainage fermé (2) Drainage ouvert (1)	74 jours
10	M.	11 mois	Drainage fermé (4) Thoracentèses (3)	38 jours
11	M.	12 mois	Médical	49 jours
12	M.	2 mois	Drainage fermé (1) Drainage ouvert (1)	68 jours
13	F.	6 mois	Drainage fermé (1) Drainage ouvert (1)	48 jours

cyanose. Ces deux symptômes résistent à l'oxygénothérapie. Il y a gonflement du thorax du même côté et distension abdominale réflexe avec vomissements. A noter que dans deux cas sur sept, nous avons été consultés d'abord pour une symptomatologie abdominale; et pour certaines raisons, il semble que l'iléus se manifeste avant les troubles respiratoires. De toute façon la poussée sous-diaphragmatique de l'iléus s'ajoutant à la poussée intrathoracique de la bulle compriment de façon alarmante ce qui peut rester de parenchyme pulmonaire sain et le résultat net constitue une véritable urgence respiratoire.

Traitement.—Le traitement d'urgence et palliatif consiste à ponctionner la bulle avec une aiguille. Ceci a été fait douze fois chez nos sept patients. Si le résultat immédiat est de courte durée, il n'en est pas moins spectaculaire. La cyanose disparaît, l'enfant respire. Il ne faut pas s'arrêter là. Il faut drainer de façon permanente avec un tube introduit dans la bulle. Si on ne le fait pas, on s'expose à

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ponctionner à toute heure du jour et de la nuit, la même bulle qui se distend sans cesse.

Parmi les méthodes connues d'introduire un tube dans une bulle, celle du trocart et la méthode ouverte, nous avons opté pour cette dernière. Sans surestimer les accidents qui peuvent survenir avec un trocart dans un thorax flexible de quatre ou six mois, il nous a été plus difficile dans un autre milieu, d'introduire ces tubes à l'aveuglette dangereuse d'un trocart. Le trocart va plus facilement dans la plèvre que dans la bulle. C'est pourquoi dans tous ces cas nous avons choisi la méthode ouverte. Nous avons fait ces drainages à la salle d'opération, endroit plus convenable et mieux préparé aussi pour donner les traitements d'urgence si le prétendu "choc pleural" survient.

Après examen radiologique de face et de profil, l'endroit le mieux approprié est choisi, badigeonné, et des champs stériles sont appliqués. L'espace intercostal est infiltré à la procaine à 1%. Une incision de deux centimètres est faite et portée en profondeur, dans la bulle même, un cathéter No. 16 ou No. 18 est introduit et connecté à un appareil à suction qui donne 15 cm. (H₂O) de pression négative. L'incision est refermée en un plan.

Cette manœuvre chirurgicale a été faite 17 fois chez nos sept patients, donc 2.5 fois par patient, en moyenne. La deuxième intubation a été faite dans une autre bulle. Il y a eu intubation bilatérale dans deux cas, et plusieurs tubes furent insérés simultanément. Chez un de ces patients, une thoracentèse d'urgence a dû être faite à mi-chemin entre deux tubes pour une nouvelle bulle qui s'était formée à la suite d'une baisse de pression dans son thorax.

Soins post-opératoires.—La tente à oxygène est toujours utilisée, de même que la suction trachéale et le drainage en position déclive. Nous donnons de l'Alévaire 30 minutes quatre fois par jour, pour favoriser l'écoulement des sécrétions. Le pédiatre prend soin de l'alimentation et des antibiotiques. Il nous demande parfois de faire une dissection veineuse à cette fin, car ces enfants sont tellement malades qu'ils en perdent leur mécanisme de tétée et qu'il faut les alimenter par voie parentérale.

Les tubes sont irrigués avec une solution stérile presque tous les jours pour en assurer le bon fonctionnement. Nous avons utilisé à l'occasion des antibiotiques dans le tube même et dans la bulle, sans observer aucun résultat évident et cette pratique a été mise de côté. A deux reprises nous avons utilisé de la varidase pour débloquer un tube; les résultats n'ont pas été concluants. Des radiographies sont prises tous les jours durant les trois premiers jours et au besoin par la suite. En moyenne, ces trois jours suffisent pour assurer la fermeture d'une bulle de façon permanente.

Il importe qu'un nécessaire à ponction pleurale soit à la main sur la table de chevet du malade. Une nouvelle bulle peut toujours survenir, comme en fait foi la pratique de 12 thoracentèses et de

17 drainages fermés chez sept patients. Dans ces cas, il faut ponctionner d'urgence.

Morbidité.—Dans trois cas, un empyème pleural nécessitant un drainage ouvert est venu compliquer l'évolution de la maladie. Dans un autre cas, une péricardite purulente à pyocyanique a nécessité une péricardiotomie. Ce même patient avait fait en outre de l'anurie pendant 36 heures et avait passé des selles contenant du sang rouge clair. Il a survécu à toutes ces complications.

Mortalité.—Nous n'avons eu aucun décès dans ce groupe de patients.

Hospitalisation.—Durée moyenne de quarante-deux jours, la plus longue étant de 74 jours et la plus courte de 9 jours.

Evolution ultérieure.—Il serait à craindre qu'une destruction aussi étendue du parenchyme pulmonaire laisse à craindre des séquelles permanentes. Jusqu'ici, nous n'en avons pas vu. Ces enfants se sont développés normalement dans la période où nous les avons observés. Cette période est courte, le cas le plus éloigné ne remonte qu'à un an et demi. Nous nous proposons de vérifier les radiographies simples, qui sont bonnes, à l'aide de bronchographie. Nous ne l'avons pas fait jusqu'ici parce que nous considérons la bronchographie comme une opération majeure chez ces bébés d'un an ou moins et nous ne croyons pas qu'une telle intervention soit justifiée par simple curiosité scientifique.

RÉSUMÉ

Treize cas de staphylococcie bulleuse ont été présentés.

Sept cas ont nécessité un traitement chirurgical d'urgence.

Le traitement a dû être répété avec une moyenne de plus de deux drainages par patient.

Nous avons insisté sur la nécessité et l'urgence de ces drainages.

Une technique a été présentée pour intuber ces bulles. Cette technique n'est pas la seule mais elle a donné d'excellents résultats entre nos mains.

BIBLIOGRAPHIE

1. FISHER, H. ET SWENSON, O.: *Pediatrics*, 20: 835, 1957.

SUMMARY

Thirteen cases of bullous infection of the lung due to staphylococcal infection in infants treated at the Hôtel-Dieu St-Vallier are described. In all cases the presence of bullae was demonstrated radiologically and in all but one case staphylococci were recovered from fluid obtained by lung puncture. The youngest patient was 2 months old and the oldest 4 years old, the average age being 9 months. There were 10 male infants and 3 females.

In 55% of cases surgical intervention was necessary. A common surgical emergency arises from the sudden expansion of a bulla accompanied by intense dyspnoea and cyanosis resistant to oxygen therapy. The thorax on the affected side and the abdomen are distended, and the case may be mistaken for an abdominal emergency. Treatment is to puncture the bulla with a needle, which relieves cyanosis and dyspnoea at once, but must be followed up by drainage through a tube introduced into the bulla. For this purpose, the open method is to be preferred to blind puncture with a trocar. Under local anaesthesia, a No. 16

to 18 catheter is introduced into the bulla through a 2 cm. intercostal incision and connected to a suction apparatus under 15 cm. of water-negative pressure.

This operation was necessary 17 times in seven patients. Postoperatively an oxygen tent is always used, together with tracheal suction and postural drainage. Alevaire was given 30 minutes four times a day. Parenteral feeding may be necessary. Antibiotic therapy is also necessary, but the

administration of antibiotics through the tube is of doubtful value, as is the use of hyaluronidase. After surgery, bullae usually close within three days, but other bullae may arise quite suddenly.

Complications included one case of empyema and one of pericarditis requiring operation. No patient died, and the average hospital stay was 42 days. So far, no after-effects of the illness have been observed in this series.

RECTAL PERFORATIONS AFTER ENEMA ADMINISTRATION

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TRAUMATIC PERFORATION of the rectum is usually a surgical emergency. The causes of perforation are numerous; occasionally they are bizarre. Experience in the Second World War led to a plan of management consisting of early laparotomy, good drainage, temporary colostomy and vigorous medical support.

Rectal perforation during the administration of an enema is a not infrequent accident. Recent experience with two personal cases led the authors to review previous cases at two local hospitals. Only three other cases of accidental rupture of the rectum were found in the admissions since 1950; two were due to enema tip injury and are summarized below, along with our cases.

CASE REPORTS

CASE 1.—This 55-year-old depressed woman was admitted to hospital on July 31, 1958. She complained of pain due to rectal prolapse. In the course of investigation, a barium enema examination was performed. It was not completely satisfactory and was repeated on August 5. Shortly after the second enema the patient became feverish, developed abdominal pain and began to vomit. She had a distended abdomen, with a question of fluid in the flanks. No bowel sounds were heard. There was minimal generalized abdominal tenderness. The patient was slightly dehydrated. The rectal prolapse was obvious. A flat film of the abdomen showed no diagnostic changes; barium was still present in the colon.

On August 6, the bowel sounds were present. The patient was passing flatus and was less distended. There was clinical and x-ray evidence of a soft mass below the umbilicus, but this was gone by the next day. On August 7, the abdomen was soft and liquid stools were passed. It was felt that there was no necessity for surgical interference at that time.

On August 15, the patient was transferred to another hospital for treatment of her mental condition. While there she was seen by a surgical consultant and a large recto-vaginal fistula was demonstrated. It was



Fig. 1—Case 1. Flat film of abdomen showing barium in the perirectal tissues.

felt that the sequence of events was, firstly, rectal perforation during barium enema; secondly, abscess formation in the perirectal tissues; and thirdly, perforation of the abscess into the vagina. A flat film of the abdomen revealed barium diffusely in the perirectal tissues (Fig. 1).

In September, a colostomy was performed on the patient. The intention was to repair the fistula later. However, her condition deteriorated and she died on October 5, 1958. Permission for autopsy was not obtained.

CASE 2.—This 59-year-old man was admitted to hospital on November 27, 1958. He complained of multiple growing subcutaneous nodules in the past two months. These were moderately tender and firm, and varied in diameter from one-half inch to several inches. There was one very large mass in the right supraclavicular area. In addition, he had lost 15 lb. over the past several months and had had some lower abdominal distress. Since the summer of 1958 he had had five to six watery bowel movements daily, occasionally containing blood. He also had a sensation of rectal fullness.

On rectal examination a large hard mass was present about 1½ inches (3.75 cm.) above the anus, involving the entire rectum. The lumen would just admit the tip of the finger.

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On December 3, 1958, in preparation for sigmoidoscopy, the patient was given an enema at 6:30 a.m. This was followed by severe rectal pain "as if something gave", and then by pain in the right upper quadrant and the right shoulder. The pain was quite severe and it hurt the patient to breathe. He also developed some abdominal guarding. This history was not known when the patient was brought down for sigmoidoscopy. He did not complain during the procedure.

After this, when the patient told us what had happened previously, a flat film of the abdomen was taken. Dilated loops of small bowel with fluid levels were seen. There was also "a large amount of free intra-abdominal air present, indicating a ruptured hollow viscus" (Fig. 2), shown best on the chest radiograph taken at this time.

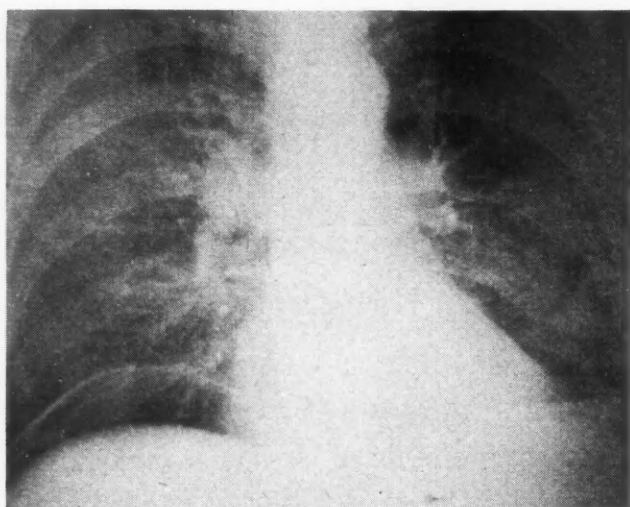


Fig. 2.—Case 2. PA film of chest: the large amount of subdiaphragmatic air can be seen on the right side; a smaller amount is also present on the left side.

In view of the history and x-ray findings, it was felt that the patient had a rupture of the rectum. Because of the widespread metastatic disease, operation was not advised. He was treated with gastric suction and antibiotics (penicillin, streptomycin and chloramphenicol). Over the next few days the patient made an uneventful recovery from his pneumoperitoneum. Suction was then removed and he was able to eat and carry on as before.

The patient received palliative radiation without any obvious effect. He died on February 14, 1959. At post-mortem examination, the large rectal carcinoma and multiple metastases were found. No evidence of rectal perforation was found at this time.

CASE 3.—This 70-year-old woman was admitted to hospital on May 7, 1956, with a provisional diagnosis of abdominal aneurysm. No history was obtainable because of a language barrier.

Physical examination revealed crepitations in both lung bases, a soft apical systolic murmur, and a pulsating midline abdominal mass. The blood pressure was 170/85 mm. Hg. On May 8, the haemoglobin value was 10.3 g. per 100 ml. (70%), red blood cell count 3.3 million and erythrocyte sedimentation rate 87 mm. Urinalysis was negative.

On May 9 abdominal aortography was done. From the level of the third lumbar vertebra to its bifur-

cation the vessel was dilated and irregular, suggesting aneurysm with clot. After aortography the patient became paraplegic; ischaemia of the spinal cord was diagnosed. Involuntary bowel movements began at this time. Over a period of a month the patient gradually recovered some function in her lower limbs.

Because some blood was noticed in the patient's stool, a barium enema examination was performed on May 18. This revealed spasm of the recto-sigmoid junction. The procedure was repeated on May 22. About three hours after the second enema the patient developed a fever and complained of feeling cold. Her blood pressure was 150/90 mm. Hg; temperature 99.3° F. By 3 a.m. the following morning the patient was confused. Her temperature reached 104.4° F, with B.P. 100/60, pulse 92 and respirations 34. One unit of blood was given. That afternoon a nurse noted that "barium returns with blood-streaked mucus from rectum". The patient did not appear acutely ill at this time, possibly because of her paraplegia.

She received antibiotics and other supportive therapy, and gradually improved. Her rectal discharge was purosanguinous on May 26. On May 28 and again on May 31, sigmoidoscopy was performed and a constricting lesion was biopsied. No malignancy was found, and the pathologist suggested that the tissue could be peritoneum.

The patient's condition was only fair. A chest radiograph on June 7 revealed extensive pneumoperitoneum. In view of this finding plus a hectic fever, an exploratory operation was advised. On June 14, the patient's condition was considered to be adequate and a laparotomy was performed. The abdominal aneurysm was covered with tantalum mesh gauze. There was a non-specific thickening in the bowel at the recto-sigmoid junction; a small perforation, sealed with left Fallopian tube, was noted. A loop-colostomy of the sigmoid colon was made.

The patient did poorly after operation. Blood pressure was below 85/50 mm. Hg and there were Cheyne-Stokes respirations. The patient died at 5:50 a.m. on June 15, 1956.

At autopsy a perforation in the anterior wall of the rectum, measuring 4 × 3.5 cm., was found approximately 3.5 cm. above the anorectal junction. The rectal wall was markedly oedematous. Creamy material appearing grossly to be barium was found in the perirectal tissues.

CASE 4.—This 65-year-old woman was admitted to hospital on October 21, 1951, complaining of crampy epigastric pain. During the investigation of this complaint, a barium and air contrast enema examination was carried out.

The radiologist's report is quoted here in its entirety: "During this procedure an extra-peritoneal rupture of the rectum occurred. This was occasioned by the necessity to use an inflated rubber bag (Bardex Enema Tip) in order to keep the contrast media in the colon as the patient was unable to retain the enema by herself. Films made shortly after the initial examination revealed air in the extra-peritoneal regions of the abdomen."

Immediately after this accident the patient was taken to the operating room. There, attempted visualization of the rupture through a sigmoidoscope failed because the rectum was full of faeces, blood and barium. At laparotomy the surface of the pararectal

and sigmoid mesentery showed many air bubbles. The anterior and lateral surfaces of the rectum showed extensive hæmatoma. A temporary colostomy was performed.

Postoperatively the patient responded well, and seemed to be making a good recovery. However, on the fourth postoperative day she had an episode of auricular fibrillation which was followed by an acute cerebrovascular accident, presumably embolic. Three days later the patient died. Permission for autopsy was not obtained.

DISCUSSION

An accurate determination of the frequency of accidental injuries to the rectum is difficult. Goldman⁹ in 1929 reported a personal case of perforation after proctoscopy; he tried to poll his colleagues to learn their experience with similar accidents, but received little information. He concluded that few of the accidents that occur are reported. In 1947, Andresen¹ sent questionnaires to 314 members of the American Proctological Society, seeking similar information; 34 physicians reported 46 cases. Andresen found another 48 cases of endoscopic rupture of the rectum in the literature.

Pratt and Jackman¹⁸ in 1945 were able to find in the literature only 18 cases of serious rectal injury by enema tips; they added two personal cases. In 1957, Large and Mukheiber¹⁵ found the number of described cases to be 31, and reported another.

These figures are a minimal estimation of incidence. Many slight injuries, where only mucosa is damaged, may go unnoticed, and many observed minor abrasions also heal uneventfully.

However, the injuries which require medical attention are serious. In 1911, Andrews² reported 15 cases of pneumatic rupture of the rectum and colon; 11 of these patients died. Of the 94 patients with endoscopic rupture reported by Andresen,¹ 45 (48%) died. The advent of the antibiotic era, plus more frequent use of colostomy, seems to have improved the prognosis. The mortality rate in the series of Large and Mukheiber¹⁵ was 25% (8 of 32 cases), while Klein and Scarborough¹³ report 50 cases of traumatic perforation of rectum and distal colon with 5 deaths (10%). More recently Murray¹⁶ in Vancouver presented a personal series of 17 cases with no deaths. All 17 patients had intraperitoneal perforations, but only three were the result of trauma (12 were associated with diverticulitis and four with carcinoma). All four of our patients died; however, only the third and fourth cases can be considered as deaths due to rectal perforation or its complications.

In most series in which all types of perforation are considered, approximately two-thirds are extraperitoneal and one-third intraperitoneal. Two of our cases, the second and third, were intraperitoneal perforations, while the other two were extraperitoneal.

There are several anatomical features of the rectal region which are of importance in the production of rectal perforations.

(a) The longitudinal axes of the rectum and the anal canal: The anal canal slants downwards and backwards from the level of the apex of the prostate, ending about one inch away at the anus. An angle is made with the rectum, which from above slants downwards and forwards. Thus an object entering the anal canal along the axis of the canal will strike the anterior rectal wall unless its direction is altered.

(b) Nerve supply: Proximal to the pectinate line the rectum is insensitive to pain. Thus it is possible to perforate the rectum during manipulation, as in giving an enema or performing endoscopy, without the patient's being aware of the accident. The immediate pain associated with most enema tip injuries is due to the concomitant injection of irritating substances into the perirectal tissues or the peritoneal cavity. Endoscopic injuries, if extraperitoneal, may be painless for hours till faecal soiling takes place.

(c) "Funnelling": Andrews² and Jones¹² have noted that the inner aspects of the thighs, the buttocks and ischial tuberosities and other tissues in this area constitute a sort of "funnel" with the anus at the apex, so that compressed air² or blunt objects¹² will be directed to the anus, and with sufficient force, into the rectum. A unique case, where a patient sat down in the water while water-skiing and sustained a rectal perforation,¹⁹ is probably a good example of this funnelling effect.

A great variety of objects have been described as producing rectal perforation. Klein and Scarborough¹³ classify these injuries as due to either external or internal trauma.

Internal trauma includes perforations during endoscopy,^{1, 4, 9, 12, 13} perforation by enema,^{12, 13, 15, 16} and a perforation by intraluminal impalement.^{13, 15} Andrews² reported a series of patients who had a compressed air source applied at or near the anus, usually as a practical joke, and who suffered a rupture of the rectum or colon. Many single case reports of unusual injuries could be classified here, but we mention only one, particularly bizarre, which must be unique: a self-inflicted perforation as a result of explosion of a fire-cracker inserted, lit, into the rectum.⁶

External trauma may result in perforation by external force, whether the result of a fall,³ during parturition,¹⁷ or associated with wounds of the buttocks,⁸ particularly in wartime. Perforation may also follow surgery on adjacent organs.¹³

Burt⁵ performed *in vitro* experiments, using normal human bowel, to determine the amount of pressure the bowel could withstand without rupturing. He found that the outer two coats of the bowel wall would rupture first, longitudinally, and the mucosa would herniate through the opening. Further increase in intraluminal pressure then

produced mucosal perforation. The average pressure before rupture of the outer two coats was 18 cm. of mercury, while that required to perforate all three layers was 21 cm. of mercury. In the administration of barium enemata, with the barium container held three feet above the patient, the pressure at the end of the tube, in the rectum, is approximately 8 cm. of mercury.¹⁴ These figures suggest that some other factor besides increased intraluminal pressure must be active in most cases of bowel perforation during barium enemata. Many of the reported cases have occurred in patients with associated rectal or sigmoid lesions.

Hartman and Hills¹¹ report two cases of rectal rupture in infants during the administration of barium enemata. In both cases the rupture was found to be longitudinal, beginning just at the peritoneal reflection. They felt that in both cases rupture was produced when the balloon and enema tip was inserted too far into the rectum before being inflated. The peritoneal reflection restricts the ability of the rectum to dilate. It is possible that the perforation which occurred in our fourth case was produced in a similar manner.

Hamit¹⁰ has reviewed the literature concerned with perforations of the rectum and colon during barium enema administration. In nearly every case definite bowel disease was present, and perforation occurred at the site of the lesion. In the second case which we report, it is probable that perforation resulted when an enema tip was pushed through an area of malignant ulceration.

TREATMENT

This has been thoroughly discussed by Chunn⁷ recently. He stresses the importance of experience gained in World War II in determining the standard therapy for this type of wound.

Extraperitoneal perforations of the rectum should be treated by performing a proximal diversionary colostomy. Posterior drainage may or may not be necessary.

Intraperitoneal rectal wounds should be closed, if possible, with two rows of interrupted non-absorbable sutures. A proximal diversionary colostomy should be performed.

In both types of injury vigorous antibiotic, electrolytic, nutritional and fluid balance supportive treatment is of great value in assuring a favourable outcome.

Careful instruction of persons who administer enemata is of the utmost importance; accurate knowledge of the anatomy of the anus and rectum is particularly necessary. The dangers of attempting to forcibly overcome resistance to the passage of the enema tube should be stressed. No inflexible enema tube need be passed more than two inches past the anus; perhaps these tubes should be fitted with guards. Finally, the radiologist should have the benefit of full knowledge of any lesions present

in the large bowel and rectum so that he can take precautions to avoid any accident, particularly in debilitated patients and those whose sensorium may be clouded.

SUMMARY

Four case histories are presented of patients who sustained traumatic perforations of the rectum while in hospital. Three of the patients were receiving barium enemata at the time of perforation, while in the fourth the rupture occurred during administration of an evacuant enema. Two of the perforations were intraperitoneal and two extraperitoneal; one patient in each group died as a direct result of the accident.

The frequency and etiology, as well as anatomical and physiological factors important in the production of rectal rupture, are discussed. Therapy should consist in early operation with establishment of proximal diversionary colostomy; this should be combined with vigorous medical support.

The authors would like to thank Drs. S. Peikoff and P. Goldstein for permission to report Case 4 and Case 3, respectively. We would also like to acknowledge the help of Miss Charlotte Stankiewicz and Miss Roma Champagne, directors of the Medical Records Department in St. Boniface Hospital and Misericordia General Hospital, respectively, and Mr. L. Stanford, Arts and Photography Department of St. Boniface Hospital, in the preparation of this paper.

REFERENCES

1. ANDRESEN, A. F. R.: *Gastroenterology*, 9: 32, 1947.
2. ANDREWS, E. W.: *Surg. Gynec. & Obst.*, 12: 63, 1911.
3. BERNSTEIN, W. C., GHENT, C. H. AND RAE, C. E.: *Minnesota Med.*, 35: 1138, 1952.
4. BORGSTRÖM, S.: *Acta. chir. scandinav.*, 104: 465, 1952.
5. BURT, C. A. V.: *Arch. Surg.*, 22: 875, 1931.
6. BUTTERS, A. G.: *Brit. M. J.*, 2: 602, 1955.
7. CHUNN, C. F.: *S. Clin. North America*, 38: 1649, 1958.
8. FEDER, I. A.: *Mil. Surgeon*, 106: 125, 1950.
9. GOLDMAN, C.: *J. A. M. A.*, 93: 31, 1929.
10. HAMIT, H. F.: *Am. Surgeon*, 21: 1226, 1955.
11. HARTMAN, A. W. AND HILLS, W. J.: *Ann. Surg.*, 145: 712, 1957.
12. JONES, J. D. T.: *Brit. M. J.*, 1: 933, 1949.
13. KLEIN, R. R. AND SCARBOROUGH, R. A.: *Am. J. Surg.*, 86: 515, 1953.
14. KLEINSASSER, L. J., AND WARSHAW, H.: *Ann. Surg.*, 135: 560, 1952.
15. LARGE, P. G. AND MUKHEIBER, W. J.: *Lancet*, 2: 596, 1956.
16. MURRAY, A. A.: *Canad. M. A. J.*, 77: 336, 1957.
17. NEELY, M. R.: *Brit. M. J.*, 2: 1288, 1956.
18. PRATT, J. H. AND JACKMAN, R. J.: *Proc. Staff Meet. Mayo Clin.*, 20: 277, 1945.
19. RABSON, L. R.: Personal communication.

RÉSUMÉ

Les lavements peuvent causer une rupture traumatique du rectum. Les auteurs présentent quatre de ces cas dont trois suivirent un lavement baryté et l'autre un lavement d'évacuation. La rupture fut intrapéritonéale dans deux cas et extra-péritonéale dans les deux autres cas. On eut à déplorer une mortalité dans chaque groupe. La fréquence exacte de ces traumatismes est difficile à évaluer, mais il est permis de croire qu'elle est plus élevée qu'on ne le pense. Trois facteurs entrent en cause dans la production de ces blessures: a-l'angle que forme l'axe du rectum et celui du canal anal favorise les lésions de la paroi rectale antérieure s'il y a introduction directe dans l'anus; b-l'insensibilité du rectum risque de masquer la blessure au moment du traumatisme; c-les cuisses, les fesses et les tubérosités de l'ischion agissent à la manière d'un entonnoir pour canaliser dans le rectum les objets contondants, les gaz et les liquides sous pression.

La traitement est fondé sur l'intervention précoce et l'établissement en amont d'une colostomie de dérivation, appuyés par un traitement médical vigoureux.

ANTIBIOTIC COMBINATIONS: A STUDY OF THE COMBINED ACTIVITY OF STREPTOMYCIN AND CHLORAMPHENICOL*

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ALTHOUGH the majority of bacterial infections encountered in clinical practice respond satisfactorily to the administration of one of a variety of antibiotics available today, a residuum of cases exists whose treatment is still unsatisfactory. These are largely problems involving fulminating infections, resistant organisms, infections in which the type of lesion produced may represent a barrier to the penetration and action of the antibiotic, and infections in which the complete eradication of the offending organism is of paramount importance for cure.

Faced by such cases the physician frequently turns to combinations of antibiotics as a possible solution to his problem, a decision which is supported in a general way by many laboratory studies in which synergism can be demonstrated when certain agents act together and in particular by the striking success of combined therapy in enterococcal endocarditis. His enthusiasm is tempered, however, by the knowledge that an equally impressive number of experimental studies have revealed that a mixture of two antibiotics may produce no more effect than the more potent member of the combination or in some cases be less effective.

Although many laboratory techniques are available by means of which the interaction of antibiotic pairs may be studied, the interpretation of the results in terms of the prediction of the effect of a particular pair when used in the treatment of a given infection is a subject of considerable dispute. The extensive review of Jawetz and Gunnison¹ gives an excellent assessment of the complex nature of this problem.

Our interest in this problem was initiated by a case of infantile gastroenteritis with septicaemia due to *E. coli* (serogroup 026). Disc sensitivity tests revealed the organism to be sensitive to streptomycin and chloramphenicol but resistant to all other commonly available agents. The child was given streptomycin and considerable improvement noted over the next 24 hours, although the patient (of course) remained very ill. Tube dilution sensitivity tests were carried out and the combined activity of the two drugs was determined by mixing equal volumes of them at a concentration of 16 times the M.I.C. of each and comparing the M.I.C. of the drugs alone with the concentration of each in the first inhibitory mixture, after the fashion of Welch *et al.*²

No interaction was noted between the components tested.

Chloramphenicol was then administered in order to decrease the risk of the emergence of a streptomycin-resistant mutant and this step was associated with rapid deterioration in the clinical condition of the patient. Death occurred some 36 hours after the beginning of chloramphenicol therapy. The results of antibiotic sensitivity tests on isolates obtained post mortem were identical with those obtained on ante-mortem cultures.

Extensive studies were then carried out on the effect of streptomycin and chloramphenicol on this strain of *E. coli* in order to attempt to correlate the results with this instance of probable antagonism.

MATERIALS AND METHODS

Streptomycin sulfate and chloramphenicol solutions were prepared in distilled water at a concentration of 1000 µg./ml., sterilized by filtration using ultrafine sintered glass filters and stored at -20° C.

Two test organisms were used, the strain of *Escherichia coli* 026 H6 noted above and a local stock strain of *Salmonella typhimurium*. Inocula were prepared by harvesting the cells from nutrient agar plates after 14-16 hours of incubation, washing them once in distilled water and re-suspending in distilled water to a standard optical density.

Test media were dispensed in 20 ml. amounts in 50 ml. flasks. After the addition of the appropriate concentration of one or both antibiotics, the flask was inoculated with the desired number of organisms and incubated at 37° C.; at suitable intervals 1 ml. aliquots were removed and viable counts performed by the drop-plate method. Each experiment was done at least in triplicate. Difco nutrient broth and agar were used throughout. All water used was double glass distilled.

RESULTS

The Combined Effect of Sub-bacteriostatic Doses of Streptomycin and Chloramphenicol on E. coli

When the two agents were allowed to act simultaneously on a relatively small initial population (10^3 cells/ml.) in doses having approximately equivalent activity but producing less than full bacteriostasis, and the growth curve was followed, more inhibition was noted with the combination than with either agent tested separately. This effect was best observed when concentrations of the antibiotics which produced minimal inhibition were combined.

The nature of this combined drug action is difficult to classify. The results might represent synergism, i.e. an effect greater than the sum of the effects of the separate agents, or might represent a simple additive action. In the latter instance not only could addition be produced by the addition of the effects of each agent on a given organism, but also, in this delicate system, the total amount of inhibition could represent the summation of the inhibition of the most susceptible fraction of the

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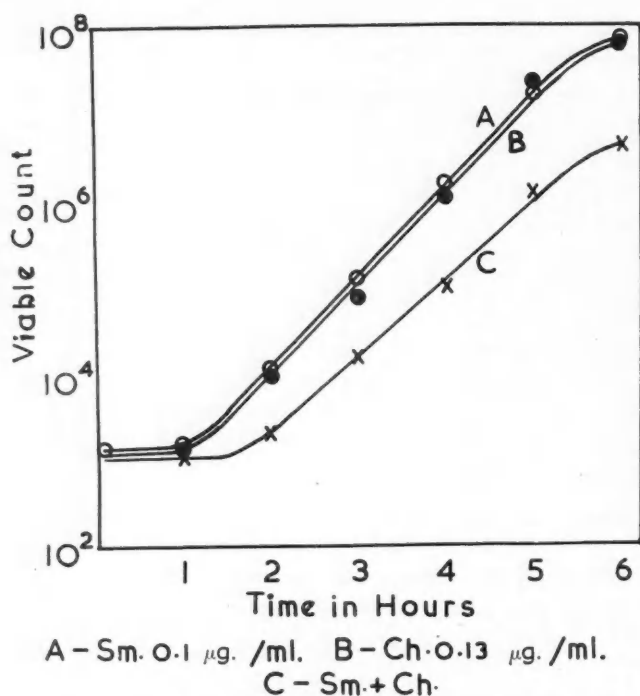


Fig. 1.—The combined effect of sub-bacteriostatic doses of streptomycin and chloramphenicol.

population, a fraction which could consist largely of different organisms with each drug.

The results recorded in Fig. 1 were obtained with concentrations of streptomycin and chloramphenicol selected as the largest doses producing no observable effect. The fact that a clearly observable effect was produced under these circumstances by the combination suggests that a synergistic action had been demonstrated.

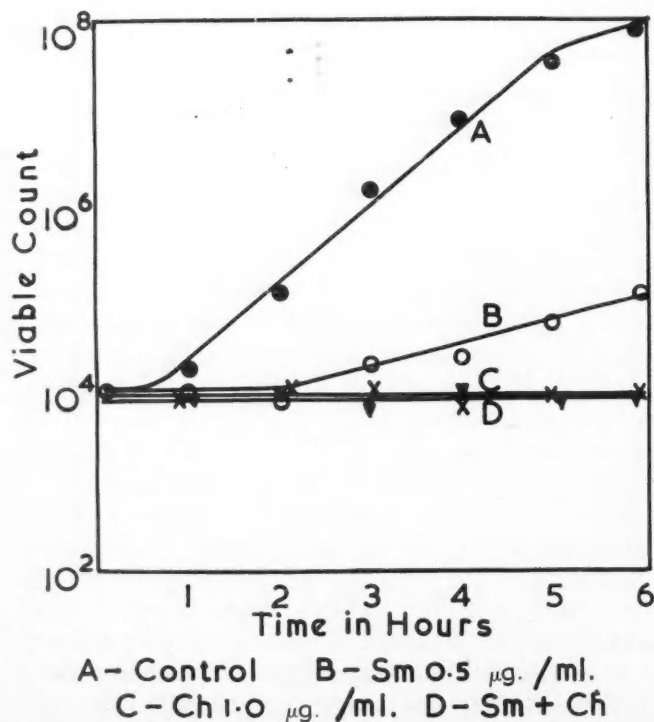


Fig. 2.—The combined effect of bacteriostatic doses of streptomycin and chloramphenicol.

The Combined Effect of Bacteriostatic Doses of Streptomycin and Chloramphenicol on *E. coli*

The results described above were observed only when the concentrations of the two agents were adjusted to produce approximately an equivalent degree of inhibition, and especially if this inhibition was minimal. When combinations were tested in which one agent produced considerably more effect than the other, the combination tended to inhibit growth to a degree equivalent to that of the more potent member. This effect, which would generally be interpreted as indifference, was most clearly demonstrated as illustrated in Fig. 2, when a fully bacteriostatic concentration of one agent was allowed to act in the presence of any sub-bactericidal concentration of the other. Full bacteriostasis was always observed. No bactericidal activity was recorded with any combination tested during the six-hour period of observation.

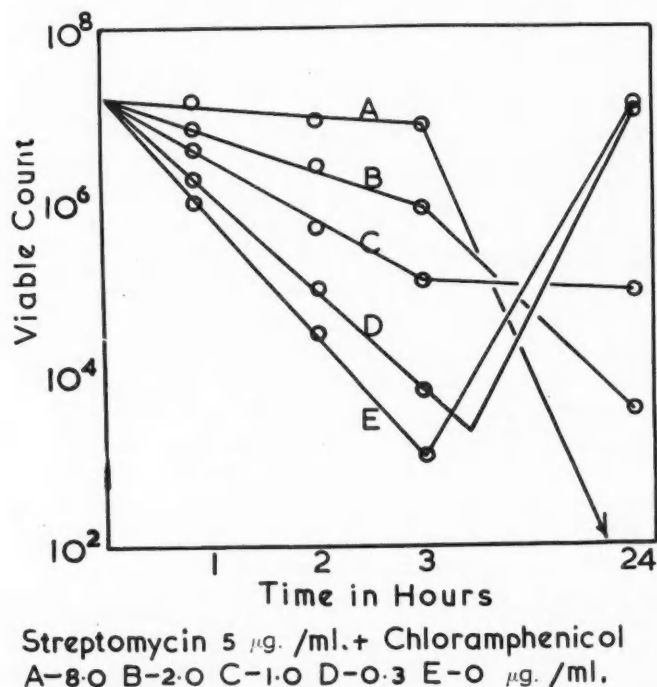


Fig. 3.—The effect of chloramphenicol on the bactericidal activity of streptomycin.

The Effect of Chloramphenicol on the Bactericidal Activity of Streptomycin

The data recorded in Fig. 3 indicate that when a large initial population of *E. coli* is exposed to an actively bactericidal concentration of streptomycin, the simultaneous exposure of this population to chloramphenicol results in a decrease in the early rate of sterilization. The degree of antagonism produced is proportional to the concentration of the chloramphenicol.

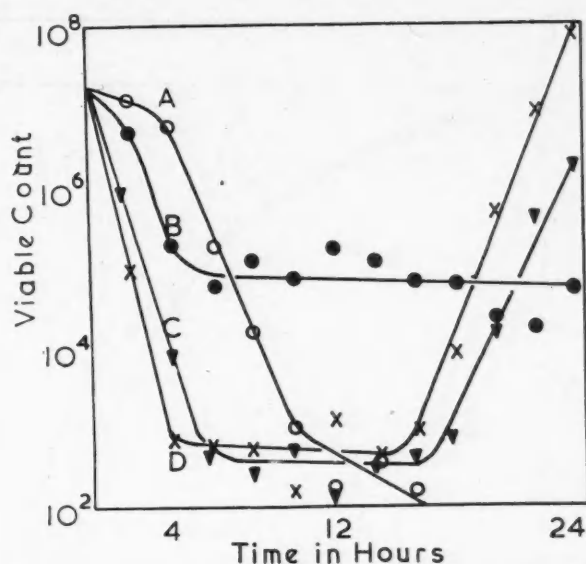
When the time of observation was extended over a period of 24 hours a number of complex effects were seen as recorded in Fig. 4. Streptomycin alone in a concentration of 5 $\mu\text{g.}/\text{ml.}$ produced a rapid bactericidal effect, the population reaching a minimum count in about four hours. A period of low

viable count then ensued until 16 hours, when the number of viable cells began to increase. Sensitivity tests performed at 24 hours indicated that streptomycin resistance had significantly increased (M.I.C. 50 $\mu\text{g./ml.}$). The period of stable population thus very likely consisted of a composite curve, the decline in viable streptomycin-sensitive cells being offset by the emergence of streptomycin-resistant organisms.

The addition of 0.3 $\mu\text{g./ml.}$ of chloramphenicol to 5 $\mu\text{g./ml.}$ of streptomycin resulted in a perceptible decrease in the early bactericidal rate, but the general course of events was about the same as that seen with streptomycin alone and the emergence of the streptomycin-resistant mutant, although slightly retarded, was not prevented. An increase in the concentration of chloramphenicol to the minimum dose shown in control trials to be fully bacteriostatic (1 $\mu\text{g./ml.}$) was associated with maximum antagonism of the total bactericidal effect of streptomycin. Not only was the early rate of sterilization decreased but also, after a period of some four hours, a state of bacteriostasis ensued and persisted for the 24-hour period of observation, and sensitivity tests showed the culture to be just as sensitive to streptomycin as at the beginning of the trial.

When the concentration of chloramphenicol was increased further, to 8 $\mu\text{g./ml.}$, maximum antagonism of the early bactericidal effect was observed. After 3-4 hours, however, rapid bactericidal activity commenced and proceeded to sterilization of the culture in 16 hours. The fact that chloramphenicol alone did not demonstrate any significant bactericidal activity in control experiments must lead one to assume that although concentrations of this agent greater than the M.I.C. do antagonize the early bactericidal activity of streptomycin to a greater extent, cell damage occurs during the action of the two agents which results finally in a bactericidal effect.

A series of effects have thus been observed when various concentrations of chloramphenicol are allowed to act in the presence of a bactericidal dose of streptomycin. Concentrations of the former agent, which are not fully bacteriostatic, antagonize the early bactericidal effects of streptomycin but do not prevent the emergence of a resistant mutant. In order to obtain the latter effect a bacteriostatic dose of chloramphenicol must be used. This, however, produces maximum antagonism of streptomycin activity. The antagonism can be largely overcome, as noted with other antagonistic pairs,³ by increasing the concentration of chloramphenicol, although it must be recorded that antagonism was invariably seen during the first three or four hours of observation regardless of the dose of chloramphenicol. The reverse, however, was not shown to be the case. Further trials indicated that the antagonistic effect of any given dose of chloramphenicol could be completely overcome by increasing the dose of streptomycin.



Streptomycin 5 $\mu\text{g./ml.}$ + Chloramphenicol
A-0.0 B-1.0 C-0.3 D-0 $\mu\text{g./ml.}$

Fig. 4.—The combined effect of streptomycin and chloramphenicol on *E. coli*.

Clearly, within a range of concentrations likely to be encountered in clinical practice, the predominant effect observed with combinations of chloramphenicol and streptomycin is antagonism of the early bactericidal action of the latter drug, and the nature of this antagonism is of some interest. The position can be held that if streptomycin acts most efficiently on multiplying cells, and it must be noted that this is a debatable point,⁴ then interference may be produced simply by the bacteriostatic action of chloramphenicol. A number of observations made during the course of this work tend to discount this hypothesis. The data in Fig. 4

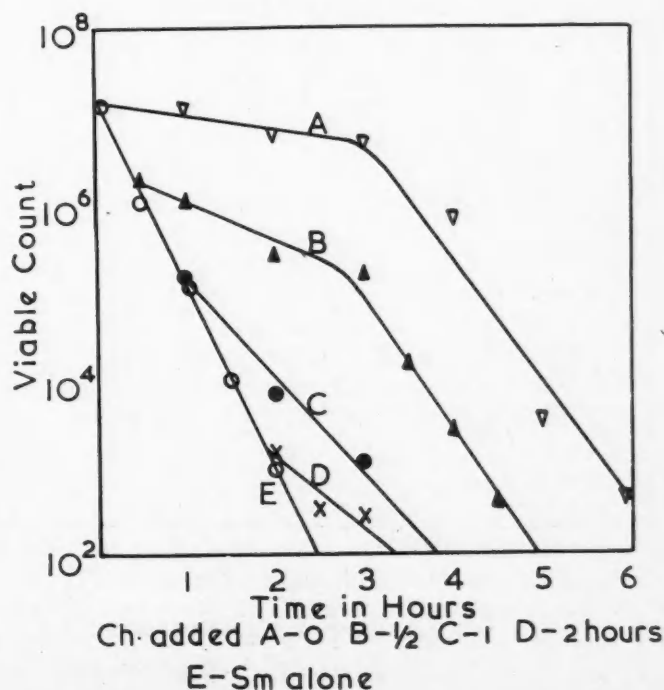


Fig. 5.—The effect of chloramphenicol on cultures previously exposed to streptomycin.

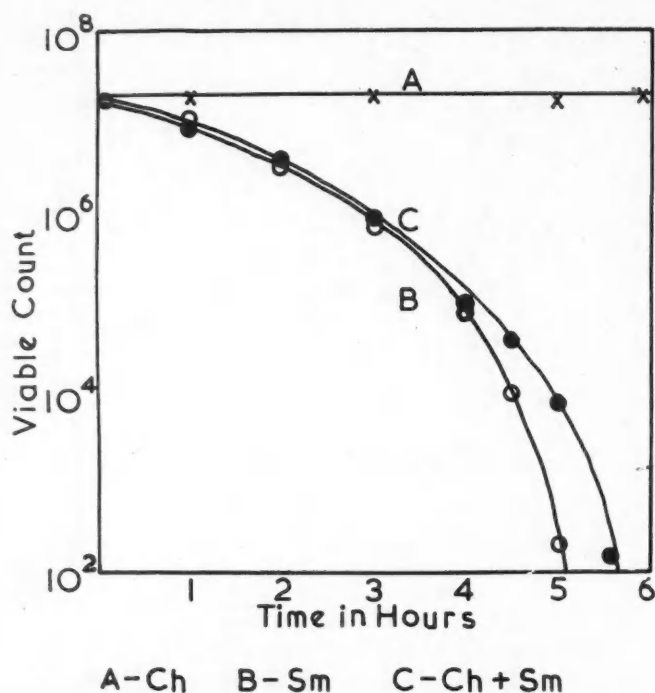


Fig. 6.—The effect of chloramphenicol on the activity of streptomycin in Tyrode's solution.

indicate that although 1 $\mu\text{g./ml.}$ of chloramphenicol produces full bacteriostasis in control experiments, doses of 2 and 8 $\mu\text{g./ml.}$ interfere to a significantly greater extent with early streptomycin activity although they can hardly be conceived to produce more bacteriostasis.

Further, it is generally held that an interfering agent must act simultaneously or before the effective agent.¹ Fig. 5 illustrates the effect of chloramphenicol on cultures of *E. coli* previously exposed

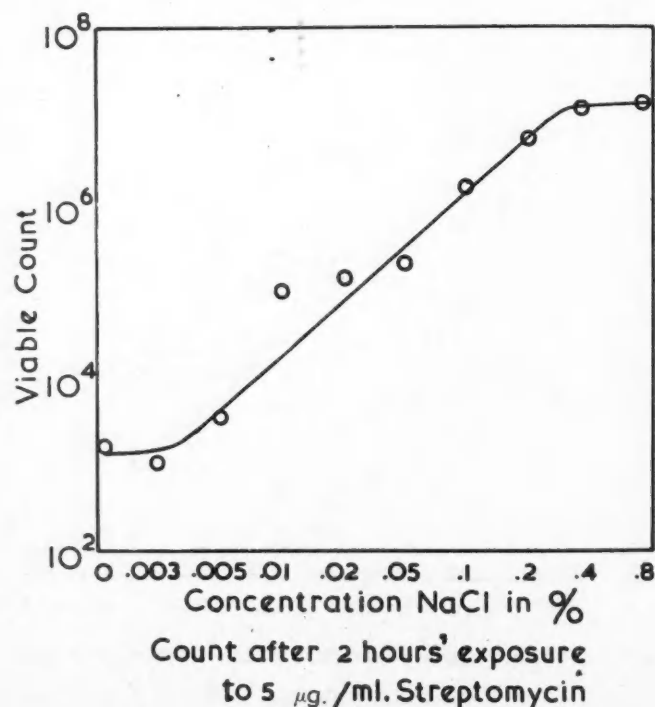


Fig. 7.—The effect of sodium chloride on the activity of streptomycin in distilled water.

to streptomycin. It is evident that chloramphenicol is capable of interrupting the bactericidal effect of streptomycin at any time during the course of action of the latter drug. This clearly must be associated with some particular biochemical disturbance produced by chloramphenicol and not a general effect of bacteriostasis *per se*.

The Effect of Combinations of Chloramphenicol and Streptomycin on Non-multiplying Suspensions of E. coli

There seems little doubt that in infected tissues the offending organism may be found in all stages of metabolic activity from rapid multiplication to near dormancy. Many workers contend that failure to eradicate organisms from the tissues in chronic infections may be due to the limited action of various antibiotics on a metabolically inert fraction of the population.⁴ A survey of the combined action of two agents thus should logically include observations on the effect of these agents on non-multiplying cells. To this end agar cultures of *E. coli* were harvested, washed twice in distilled water and suspended in Tyrode's solution in the presence of the test agents. The results over a six-hour period of observation are recorded in Fig. 6. Chloramphenicol (100 $\mu\text{g./ml.}$) produced no observable effect. Streptomycin (5 $\mu\text{g./ml.}$) produced a distinct bactericidal effect although the rate was clearly less than that noted with the same dose of this agent in broth, especially during the first three hours. The two drugs together produced, in general, the same effect as streptomycin alone with a slight retardation of the bactericidal rate during the later phases of observation. The absence, however, of unequivocal antagonism is in agreement with the observations of Jawetz *et al.*,⁵ who suggested at the time that this result was due to the fact that the cells were not multiplying. The decreased early activity of streptomycin in balanced salt solution has been presented as evidence that streptomycin has its most profound effect on actively multiplying cells. It should be borne in mind, however, that tests carried out in broth and salt solution will be influenced, not only by the metabolic activity of the cells, but also by the effects of the various components of these media on the activity of streptomycin. The influence of sodium chloride concentration on the activity of streptomycin is recorded in Fig. 7. The antagonism is quite evident. Various investigators have observed that a number of salts, including sodium chloride, markedly decrease streptomycin activity.^{6,7} Berkman *et al.*⁶ have noted, in this respect, that part of the mechanism of action of streptomycin is adsorption at the surface of susceptible cells. The affinity of streptomycin for bacterial cells has been shown by these workers to be greatly reduced in the presence of sodium chloride. Tests of streptomycin activity in balanced salt solution thus differ from

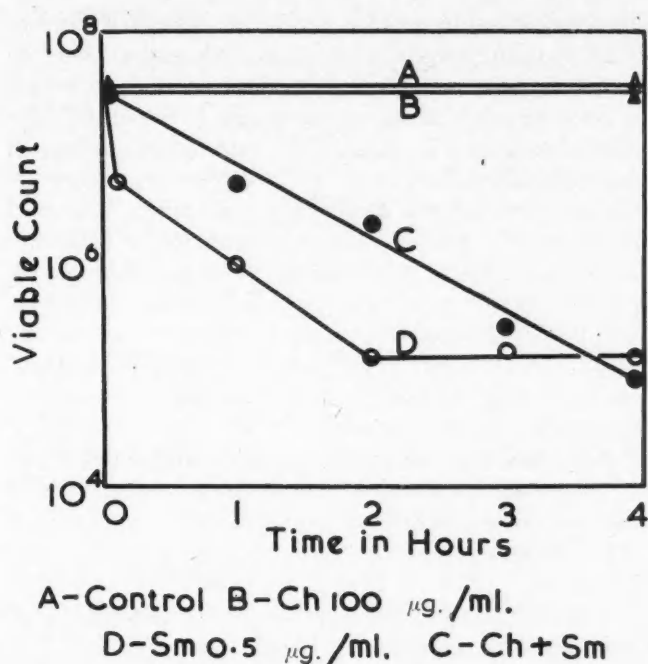


Fig. 8.—The effect of chloramphenicol on the activity of streptomycin in distilled water.

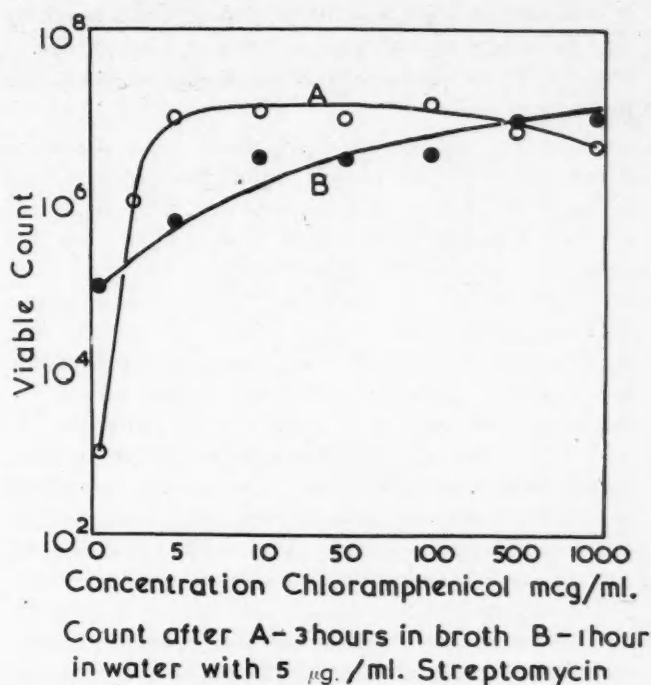


Fig. 9.—The effect of chloramphenicol on the activity of streptomycin in water and broth.

similar tests in broth not only in that the cells are not multiplying, but also in that the former medium consists predominantly of antagonistic concentrations of salt. Further, Gunnison *et al.*⁴ noted that in trials carried out in Ringer's solution their test organisms tended to die out rapidly in the absence of drugs. Although no change in viable count was noted in our trials with washed cells in Tyrode's solution during the six-hour period of observation, counts carried out at 24 hours indicated that a significant proportion of the population had failed to survive. The probability exists, therefore, that the action of streptomycin in balanced salt solution may be further modified owing to the fact that the drug is acting on cells suspended in a medium in which they not only cannot multiply but also are slowly sterilized. The combined activity of streptomycin and chloramphenicol in Tyrode's solution is thus influenced by a complex of factors and our inability to obtain a result similar to that noted in broth is not surprising.

Fig. 7, aside from demonstrating the antagonistic action of salt, shows that in concentration of sodium chloride below 0.003%, 5 µg./ml. of streptomycin produces in two hours a reduction in count greater than that noted in broth (Fig. 3), an observation supported by the work of Gunnison *et al.*⁴ The effect of chloramphenicol on the activity of streptomycin in distilled water is depicted in Fig. 8. Streptomycin in a concentration of 0.5 µg./ml., a dose which is seen in Fig. 2 to be sub-bactericidal in broth, is seen to produce a curve of bactericidal effect distinctly different from that noted in broth. A very rapid drop in viable count is observed during the first two hours of exposure, after which a more leisurely decline takes place. Chloramphenicol is seen to antagonize the early effects of streptomycin in this medium although

after three to four hours the viable counts obtained with streptomycin alone and in combination with chloramphenicol were practically identical and declined together over a further eight hours.

Subsequent trials indicated that demonstrable antagonism was confined to the early period of rapid bactericidal activity of streptomycin and that this antagonism, like that in broth, was proportional to the concentration of chloramphenicol but over a much wider range (Fig. 9). Counts performed after four to six hours' exposure to the various combinations and to streptomycin alone were never significantly different, a form of indifference in drug interaction.

Again one cannot consider the results in broth and distilled water to differ only in terms of the metabolic activity of the test cells. Streptomycin acts in distilled water on organisms suspended in a medium unsuitable for their simple survival so that the rate of sterilization consists of at least two components, the effect of the drug and that of the suspending fluid. The early bactericidal effect is most likely a measure of specific streptomycin activity, but again this is probably modified due to the fact that a minor degree of biochemical disturbance, which would be sublethal in broth, may give rise to a bactericidal effect if it upsets those essential mechanisms which serve to maintain the integrity of the cell against the substantial osmotic insult produced by distilled water.

The fact that antagonism, limited though it may be, is clearly demonstrable in distilled water, indicates that some specific action of chloramphenicol interferes with those circumstances suitable for the optimal activity of streptomycin. It is also perfectly clear that streptomycin is capable of sterilizing non-multiplying cells, although whether

it will do so and how its action is influenced by the presence of chloramphenicol is dependent in large part on the constitution of the surrounding medium.

A variety of effects have thus been observed when streptomycin and chloramphenicol were allowed to act simultaneously on this strain of *E. coli*. The particular effect observed at any one time was profoundly influenced by the nature of the medium, the relative and absolute concentrations of the agents and the time of observation. Bacteriostatic concentrations acting on multiplying cells were largely associated with indifference, i.e. the action of the combination was equivalent to that of the most active component. Careful adjustment of drug concentrations at a sub-bacteriostatic level did, however, give rise to what appeared to be a synergistic effect. The early bactericidal activity of streptomycin was unequivocally antagonized by chloramphenicol. Minimum but fully bacteriostatic doses of the latter agent were associated with maximum prolonged antagonism, whereas with larger doses, although early antagonism was more pronounced, an effective bactericidal action was later resumed. Chloramphenicol was also observed to inhibit the emergence of streptomycin-resistant mutants. Antagonism was further demonstrable when the two agents acted together on non-multiplying cells in distilled water. This interference was noted, however, only during the first few hours of exposure and was not observed in balanced salt solution. Later observations in both media revealed the combination to produce an effect approximately equivalent to that of streptomycin alone.

The application of the preceding data to the prediction of the effect of this combination of agents when it is used therapeutically is extremely difficult. The size of the dose and the relative rates of absorption, distribution, metabolism and excretion will give rise to a wide variety of combinations of concentrations in various tissue locations at any particular time. These relative concentrations will change with time and will act on organisms of varying metabolic activity in sites in which physicochemical conditions may differ to a remarkable degree. Clearly, then, no single test can describe the total possible effects of a combination of agents and, in the experiments described, the effects of a number of important variables such as pH, eH and organic acid concentration have not been ascertained. However, one gains the general impression that when bactericidal concentrations of streptomycin are attained, any significant concentration of chloramphenicol will antagonize the early activity of the former agent. Maximum antagonism can be associated with no less than full bacteriostasis. If a concentration of either agent is attained which is bacteriostatic, then at least this level of bacteriostasis will be produced by the combination. It would seem not unreasonable to suppose that the interference of chloramphenicol with the action

of streptomycin could only be observed in an infection in which a bactericidal action was of prime importance. Certainly, the instances in which a positive correlation can be made between *in vitro* measurements of combined activity in terms of bactericidal effects and *in vivo* results in human disease are largely confined to subacute bacterial endocarditis, a disease in which bactericidal action appears to be a prerequisite of a suitable therapeutic agent. A great many infections, however, will respond satisfactorily to treatment with essentially bacteriostatic agents and in these infections the antagonistic action of chloramphenicol would probably not be observed.

A convenient laboratory model suggested itself as a test of the above generalization in the form of experimental infections in mice with *E. coli* and a *Salmonella* species.

The Effect of Combinations of Chloramphenicol and Streptomycin on E. coli Infections in Mice

Mice weighing approximately 25 g. were challenged intraperitoneally with 0.2 c.c. of a 1 in 4 dilution of an overnight shaker culture of the strain of *E. coli* used in the above work. Immediately after challenge they were divided into four groups, one treated with a single dose of streptomycin, one with chloramphenicol, one with both agents and one untreated group. All drugs were administered intramuscularly. The data obtained from several experiments are drawn together in Table I. The concentrations of the antibiotics were

TABLE I.—THE EFFECT OF A COMBINATION OF STREPTOMYCIN AND CHLORAMPHENICOL ON *E. COLI* INFECTION IN MICE

Streptomycin dose in µg.	Chloramphenicol dose in µg.	% of 60 animals dead at			% Survivors
		16 hrs.	24 hrs.	48 hrs.	
0	0	51.7	73.3	83.3	16.6
100	0	43.3	70.0	78.3	21.7
0	250	25.0	51.7	61.7	38.3
100	250	23.3	48.3	60.0	40.0
0	0	63.3	83.3	90.0	10.0
0	250	36.7	55.0	65.0	35.0
250	0	6.7	8.3	10.0	90.0
250	250	6.7	8.3	8.3	91.7

adjusted so that in the first part of the table the effect of chloramphenicol is greater than that of streptomycin, whereas the reverse holds in the second part. Inspection of the data reveals that the therapeutic effect of the combination of agents is equivalent to the effect of the more potent member of the pair, a type of interaction generally referred to as indifference.

The Effect of Combinations of Chloramphenicol and Streptomycin on Salmonella typhimurium Infections in Mice

One of the problems of combined antibiotic therapy is the fact that the results obtained in *in vitro* assays with a given pair of agents and a given organism cannot be applied to other species. In most instances varied results will be obtained even when a number of strains of the same species are tested. Considerable preliminary work was thus

TABLE II.—THE EFFECT OF A COMBINATION OF CHLORAMPHENICOL AND STREPTOMYCIN ON *SALMONELLA* TYPHIMURIUM INFECTION IN MICE

Challenge dose	Drug administered	% of 60 animals dead at hours						% Survivors
		16	24	48	72	96	108	
4.0 x 10 ⁷	None	90	100	100	100	100	100	0
4.0 x 10 ⁷	Chloramphenicol	83.3	86.7	98.3	100	100	100	0
4.0 x 10 ⁷	Streptomycin	60	60	75	75	80	80	20
4.0 x 10 ⁷	Streptomycin + chloramphenicol	81.7	85	85	90	90	90	10
2.4 x 10 ⁶	None	60	75	98.3	98.3	98.3	98.3	0.7
2.4 x 10 ⁶	Chloramphenicol	10	31.7	45	50	58.3	65	35
2.4 x 10 ⁶	Streptomycin	0	0	0	6.7	21.7	26.7	73.3
2.4 x 10 ⁶	Streptomycin + chloramphenicol	3.3	16.7	33.3	33.3	43.4	50	50

Each antibiotic was administered in a dose of 800 µg.

necessary before proceeding with the next aspect of this project. The stock *Salmonella* strains held in this laboratory were surveyed and a series obtained having approximately the same tube sensitivity as the strain of *E. coli* used in the above studies. We were fortunate in finding among this series a culture of *Salmonella typhimurium* which on extensive testing demonstrated the same general reactions to combinations of streptomycin and chloramphenicol as those previously described. Mice were challenged intraperitoneally with this strain and treated by a single intramuscular injection of streptomycin, chloramphenicol or both in the same fashion as the experiment with *E. coli*. The results recorded in Table II demonstrate a distinct antagonistic effect. The number of survivors in the group treated with the combination, although in general greater in number than those in the chloramphenicol-treated group, are clearly fewer than the number surviving after treatment with streptomycin alone.

DISCUSSION

The results of tests of the combined activity of two antibiotics would appear to be strongly influenced not only by the nature of the agents and the organism tested, but also by the conditions of the test, i.e. the relative and absolute concentrations of the antibiotics, the metabolic activity of the test cells, the composition of the test medium and the time of observation. Appropriate manipulation of these test conditions has allowed the observation of a whole series of effects with combinations of streptomycin and chloramphenicol.

1. A form of synergism when carefully selected sub-bacteriostatic doses were used.

2. Indifference over a wide bacteriostatic range of concentrations.

3. Antagonism of the early bactericidal effects of streptomycin. This interference by chloramphenicol would appear to be a specific effect of the activity of this agent, independent of the time of exposure of the cells to streptomycin, and may be in large part overcome by very large doses of either agent.

4. Prevention of emergence of streptomycin-resistant mutants by chloramphenicol.

During the course of treatment of a systemic infection with such a combination of agents, it appears most likely that all of these interactions occur at different times and in different tissues. Thus, having ascertained to a limited extent the types of interactions which may occur, it is left for us to consider what interactions are likely to occur in an infected individual to an extent sufficient to influence the outcome of therapy.

The limited form of synergism demonstrated with minimal doses requires such a critical balance of conditions for its demonstration that it can hardly be conceived to be a reaction of practical significance, although it is clearly of theoretical interest. The ability of chloramphenicol to prevent the emergence of a streptomycin-resistant mutant would appear to be a feature which may have direct, although limited, application. The two outstanding characteristics of this drug pair with the organisms tested are indifference at bacteriostatic levels and antagonism when bactericidal concentrations of streptomycin are attained. Considering that antibiotics are generally used in adequate dosage so that bacteriostatic concentrations of chloramphenicol and bactericidal concentrations of streptomycin are achieved, whether these interactions will influence the results of treatment of a given case would appear to be dictated largely by the nature of the infection being treated. This is well illustrated by the animal experiments. *Salmonella typhimurium* is a virulent mouse pathogen, capable of maintaining itself in the animal's tissues in relatively small numbers, multiplying, invading, and producing death. The natural resistance of mice, which have had no experience with this organism, is of a relatively low order so that if a bacteriostatic agent is applied for a limited period of time, as in our single-dose experiments, a large percentage of the infecting population will remain viable and, when the antibiotic effect declines, will be fully capable of multiplication and invasion. The success of very short term therapy rests on the ability of the antibiotic to reduce effectively the population of pathogens to a sublethal level by its bactericidal activity. The ability of chloramphenicol to interfere with the early bactericidal effect of streptomycin can thus be demonstrated as in Table II.

The nature of *E. coli* infections in mice is considerably different. This organism has a very limited ability to produce fatal infection. The lethal dose of viable cells is generally only slightly smaller than that of killed cells. Death commonly occurs within a few days of challenge or not at all and the development of slowly progressive infection is not seen. If a bacteriostatic agent is applied to an infecting population of *E. coli* even for a limited period, time is made available for the natural mechanisms of resistance to reduce effectively this population to the small degree necessary to eliminate its lethal potential. It is thus probable that fully effective bacteriostasis is associated, in this infection, with a maximum observable effect and under these conditions the fact that the bactericidal action of streptomycin may be reduced to a bacteriostatic effect by the concomitant activity of chloramphenicol is not of therapeutic importance, as illustrated in Table I.

One realizes that the interpretation of the type of data presented, in terms of the treatment of human disease, is a hazardous undertaking. The total therapeutic effectiveness of an antibiotic is influenced by so many variables that in general the only positive method at the present time of comparing various agents is by carefully controlled clinical trial. However, it would seem not unreasonable to hold that with streptomycin and chloramphenicol, or a similar pair which gave the same type of interaction *in vitro*, if the infection being treated was one in which a bactericidal effect was essential, one might expect to observe evidence of antagonism when the two agents were used together. The circumstances in which a bactericidal effect is essential for effective therapy are, of course, limited. The clearest example is that of subacute bacterial endocarditis, and it is interesting to note that it is with this disease that the most striking correlations have been made between *in vitro* tests and clinical results.⁸

Another instance may be that of the fulminating infection. A patient may be conceived of as reaching a stage at which the total population of pathogens in the body has reached a critical level so that a minor increase is sufficient to attain a lethal effect. The successful treatment of such a case with a bacteriostatic agent would require the maintenance of full bacteriostasis for several days in order to prevent any increase in the total bacterial population in the tissues. A bactericidal agent is more likely to be effective under these conditions, in that although a given dosage schedule may not be sufficient to control the entire population of pathogens, the total number of organisms may be significantly reduced over a short period and the immune mechanisms of the body given time to exert their effect. The case of *E. coli* septicaemia reported at the outset of this paper may have been such a case. The bactericidal action of streptomycin may have been essential to survival and the addition of the interfering agent largely

responsible for the fatal result. It is not meant by this to imply that bactericidal agents are in general to be considered the drugs of choice in the treatment of an infection. The superiority of chloramphenicol in the treatment of typhoid fever, for example, seems beyond question. This does imply, however, that there may be stages of infection in which a particular bactericidal agent may have a life-saving effect although the final treatment of a given disease may rest with another drug.

Another point of view which appears to be tenable is that with streptomycin and chloramphenicol or a similar pair, if the infection being treated is one which would respond equally well to either agent, then one could expect to achieve no greater effect by the administration of both agents. The authors are impressed by the probability that this is the commonest result of combined antibiotic therapy. In examining the multitude of reports now available on clinical trials with combined antibiotics, one is struck by the frequency with which two types of studies occur. One of the commonest types is that in which the results of treatment of a variety of infections with a given combination is recorded, no attempt being made to determine the comparative efficiency of the components of the combination. The absence of the latter data allows only one reasonable interpretation of such a study, that the combination had a measurable degree of antimicrobial activity *in vivo*. The crucial question whether the combination demonstrated more, less, or the same therapeutic effect as any one of its components is left unanswered. Another common approach is to report the results of treatment of a series of patients with the same class of infection, generally urinary tract or wound infections, with a combination of agents without regard for the specific organisms involved. There seems to be little to be gained by belabouring the point that in a given series of wound infections the routine administration of a mixture of penicillin and streptomycin will give better results than the routine administration of penicillin alone. The fact that a given number of cases of wound infection, subsequently shown to be caused by enteric organisms, did not respond to routine penicillin therapy does not constitute evidence of failure of penicillin therapy and the superior efficiency of the drug combinations but evidence of the improper use of penicillin and the effectiveness of streptomycin in these cases. The critical data would clearly be a comparison of penicillin and this drug with streptomycin in the treatment of a series of infections due to penicillin-sensitive organisms or alternatively the frequently hoped-for but rarely achieved situation in which a good result is obtained with a given combination in an infection which does not respond satisfactorily to the administration of either member of the pair alone. Further, this type of study implies as desirable the approach to infections of treatment without diagnosis, a violation of a principle

generally held to be the cornerstone of intelligent therapy.

Antibiotic pairs are ordinarily used with the hope of obtaining an enhanced degree of activity. One can only agree with McDermott⁹ that the instances in which this hope has been satisfied in human infections are remarkably few. So limited are the number of proven instances in which antibiotic synergism can be demonstrated that one is left with the conclusion that only certain drug combinations acting on certain species can produce this effect, and that only in certain specific types of disease does this effect become of therapeutic importance. The basic need for laboratory tests which will usefully predict the degree of effectiveness of an agent in a given infection is self-evident. Until the remarkable advances which have been made in the description and understanding of the *in vitro* activity of antibiotics are matched by carefully controlled clinical trials with which such data may be correlated, antibiotic therapy will remain a purely empirical form of treatment.

SUMMARY

An extensive laboratory study has been presented in an attempt to correlate experimental measurements of the combined action of streptomycin and chloramphenicol with an instance of probable antagonism when these two agents were used in the treatment of a case of *E. coli* septicaemia.

A wide variety of effects were obtained when streptomycin and chloramphenicol were allowed to act simultaneously on this strain of *E. coli*. The particular effect observed at any one time was profoundly influenced by the nature of the medium, the relative and absolute concentrations of the agents and the

time of observation. Two predominant effects were observed. Combinations at bacteriostatic concentrations were associated with indifference whereas combinations of chloramphenicol with bactericidal concentrations of streptomycin demonstrated distinct antagonism.

The problem of the application of these data to the treatment of human infection is discussed and illustrated by animal experiments in which both indifference and antagonism were demonstrated.

REFERENCES

1. JAWETZ, E. AND GUNNISON, J. B.: *Pharmacol. Rev.*, 5: 175, 1953.
2. WELCH, H. et al.: *Antibiotics Annual* 1957-1958: 738, 1958.
3. JAWETZ, E. et al.: *J. Bact.*, 64: 29, 1952.
4. GUNNISON, J. B. et al.: *J. Gen. Microbiol.*, 13: 509, 1955.
5. JAWETZ, E. et al.: *A.M.A. Arch. Int. Med.*, 87: 349, 1951.
6. BERKMAN, S., HENRY, R. J. AND HOUSEWRIGHT, R. D.: *J. Bact.*, 53: 567, 1947.
7. KLEIN, M. AND KIMMELMAN, L. J.: *Ibid.*, 52: 471, 1946.
8. PILKINGTON, T. R. E., ELEK, S. D. AND JEWELL, P.: *J. Lab. & Clin. Med.*, 47: 562, 1956.
9. MCDERMOTT, W.: *Chemotherapy of microbial diseases, In: Bacterial and mycotic infections of man*, 3rd ed., edited by R. J. Dubos, J. B. Lippincott Company, Philadelphia, 1958, p. 694.

RÉSUMÉ

Les auteurs ont entrepris une étude de laboratoire afin de déterminer de manière quantitative l'action combinée de la streptomycine et du chloramphénicol—y compris l'antagonisme probable de ces deux substances telles qu'elles furent employées dans le traitement d'un cas de septicémie à colibacille. Un grand nombre d'effets différents fut obtenu lorsque la streptomycine et le chloramphénicol furent mis en présence simultanément de cette souche de colibacille. Ces effets ont toujours été influencés par la nature du milieu de culture, les concentrations relatives et absolues d'antibiotiques et l'horaire des observations. Il existe deux effets dominants. Lorsque les produits se trouvaient en concentration bactériostatique leur action réciproque était indifférente mais lorsque le chloramphénicol se trouvait en présence de concentrations bactéricides de streptomycine l'antagonisme très net s'établit. L'application de ces données au traitement des infections humaines est illustrée par l'expérimentation animale au moyen de laquelle on peut démontrer l'indifférence et l'antagonisme.

THE CORRECTION AND PREVENTION OF DEFORMITY IN RHEUMATOID ARTHRITIS ACTIVE IMMOBILIZATION*

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WHEN WE see a patient crippled with rheumatoid arthritis, do we often ask ourselves in detail how he got that way? Are ankylosis and deformity of joints inevitable, or can they be avoided?

A careful history usually provides us with the answers. Four out of five bedridden patients will relate the same sequence: (1) his knees were swollen and painful and his quadriceps muscles wasted away; (2) he walked less and less, and sat in an armchair more and more; (3) he could

not straighten his knees; (4) he could not walk and took to his wheelchair or bed; (5) his arms became fixed and his hands powerless.

He becomes bedridden for one reason only: he has a flexion deformity of both knees. If he can straighten one knee, he will continue to walk. Pain in the feet and ankles may be troublesome, but it does not confine him to bed for long. Even ankylosis of both hips does not prevent the patient from walking. These simple facts may be forgotten when the patient has been immobile for years with fixed and deformed joints.

While he can dress himself daily and walk around the house, the patient will do enough to keep his muscles active and his other joints mobile. When he cannot walk, he lies or sits with his arms at his side, elbows flexed, forearms pronated and wrists dropped. Rest in bed is disastrous to joints, bones and muscles. Muscles become wasted, bones decalcified and joint capsules fibrosed. The feet will

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lose their shape if they do not bear weight; joint cartilage will lose its vitality. Its posture results from a delicate balance of the muscular pulls and the external forces which act on a joint. When the patient lies down, the force of gravity is removed and certain muscular pulls remain unopposed; thus the joints of a recumbent patient readily occupy new positions.

In rheumatoid polyarthritis most of the pain is felt in the hands and the feet, and every patient is in great fear of two things: (1) that he will not be able to use his hands; (2) that he will not be able to walk. He can be certain, however, that he will be able to walk so long as he can straighten his knees. And he can be certain that he will use his hands as long as he prevents them from dropping.

He should never be sent to hospital merely for a rest, and he should be kept out of bed if possible. If he has to go to bed for another purpose (e.g. an operation), he should keep his knees extended, and as soon as possible he should get out of bed every day and walk. Deformities may occur even after the arthritis has been suppressed, because the muscle balance has not been restored. Weakness of extensor muscles should be watched for and guarded against; a serious disability may follow a few weeks of neglect of this precept.

THE WRISTS

More pain is felt in arthritic hands than in any other joint, and in the majority of cases the pain comes from the wrist. Most of the swelling may be on the dorsum of the hand, and the fingers may straighten and droop. The hand cannot be closed or supinated; the elbow and the shoulder are held to the side, and the whole arm may become fixed.

Usually the swelling of the hand is due to a local cause—arthritis of the wrist. We know from experience that a furuncle or a septic infection in the area of the wrist may cause swelling of the whole hand. Arthritis of the wrist may do the same. The painful hand may be diffusely tender to palpation, but acute tenderness will usually be confined to the volar surface of the wrist (Fig. 1). If the arthritic inflammation is chiefly on the volar aspect, swelling on this side is prevented by the transverse carpal ligament. Pain may be referred wholly to the fingers.

If the median nerve is involved in the inflammation, the fingers may be numb. In most cases diagnosed as carpal canal syndrome, the basic lesion is arthritis of the wrist, and the symptoms can be relieved by immobilization.^{4, 13}

Diagnosis of arthritis of the wrist is extremely important and depends on the recognition of localized tenderness. Irreparable harm may be done by allowing a painful wrist to droop in pronation for a few weeks. This can be avoided if the wrist is fixed in the correct position and the fingers and thumb are left free. Pronation and supination will be unhampered if the cast is applied with the wrist



Fig. 1.—Shaded areas indicate localized tenderness in arthritis of wrists.

midway between supination and pronation and the styloid processes of the radius and ulna are padded with felt (Fig. 2).

As soon as the wrist has been fixed, the pain in the fingers is much reduced. It usually disappears within 12 hours, and the patient can use his hand. If he uses his hand he must use his whole arm, and the elbow and shoulder usually improve. After three weeks the plaster is removed, and a leather support or a plaster cast is worn intermittently. Even if it is discarded during the day, it should be worn at night for a long time (Fig. 3).

Ankylosis of the wrist never follows unless the cartilage has disappeared, when a stable arthrodesis is a good result. Rotation of the forearm is always preserved even when the wrist is ankylosed.

When the wrist is not splinted, the patient should be instructed to prevent it at all times from drooping in pronation. When resting, it should be either



Fig. 2.—Plaster casts applied continuously which allow full closure of hand and full rotation of forearms. When the transverse bands are cut away, cast can then be applied intermittently.

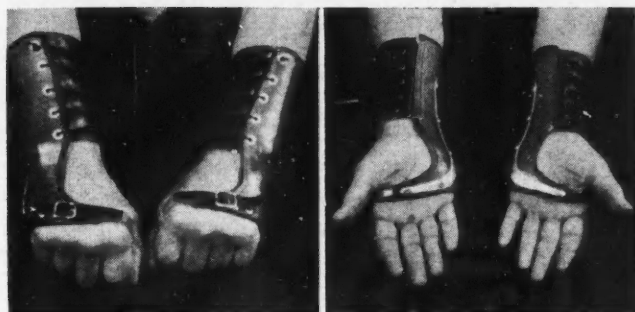


Fig. 3a

Fig. 3b

Fig. 3, a. and b.—Leather supports strengthened with metal, which allow full closure of hand and full rotation of forearm.

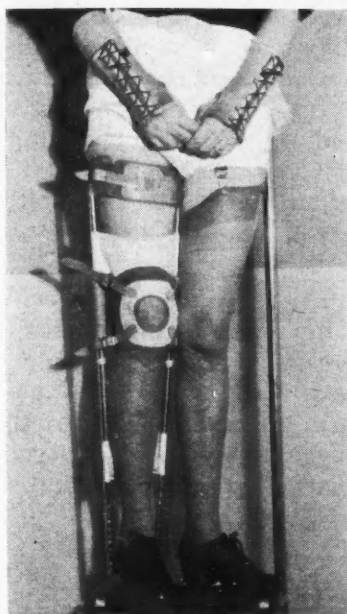


Fig. 4.—Band caliper to suppress inflammation of knee and allow weight-bearing (note supports on wrists).

splinted or allowed to hang in supination. Gripping and twisting exercises should be done.

The same method may be used for acute attacks of arthritis in the metacarpo-phalangeal or inter-

phalangeal joints.⁷ But the wrist is more important, because it is a focus or springboard from which arthritis spreads to involve other joints.⁶ If polyarthritis is aborted in the wrist, it often leads to a complete remission of the disease.

THE KNEE

The knee is another joint from which polyarthritis is likely to spread.⁶ The process, as it flits from joint to joint, merely touches most of them but it is likely to settle in the knee, which may become acutely inflamed and threaten to cripple the patient.

The knee which has become such a threat may be painful or painless, swollen or not swollen, able to be flexed or not. But it always has a weakened quadriceps which needs strengthening. Flexion must be avoided and the patient should concentrate on quadriceps drill. He should keep the knees straight when he is sitting or lying, and his chairs and bed should be raised on blocks to more than 22 inches. Physical treatment which puts the joint through its full range of flexion does harm by further damaging the inflamed synovial membrane.

A very weak quadriceps may be supported by a cylindrical plaster cast (Fig. 5a) or a straight caliper with a band at the top instead of a ring (Figs. 4 and 5b). The leg bears its own weight; walking is encouraged to strengthen the muscles and to preserve the articular surfaces. If the knee is not painful or swollen, the caliper or cast may be removed at night; in most cases it is better to wear it continuously for a week or two. Quadriceps drill should be persistent.

If the knee is painful and swollen, the caliper or cast is applied, with the leg straight, for three weeks. Both knees can thus be treated at once, and the patient uses crutches (Figs. 5a and 5b). The pain disappears forthwith and the swelling subsides rapidly, even though the limb is bearing weight. After three weeks the caliper is left off for two hours each day. This period gradually lengthens, and after two months the patient is wearing the caliper at night only. If he cannot sleep in it, it should be worn during the day for a few hours. The quadriceps usually needs support for a few hours every day for six months.⁷

Flexion always returns with ordinary use of the limb, and it should not be sought by forcible active or passive movements. Quadriceps exercises should be performed, and low chairs should be avoided. There is no danger of ankylosis in extension unless the cartilage has disappeared—when ankylosis is a happy result.

IF THE KNEE CANNOT BE EXTENDED

If the patient cannot straighten his knee, it can usually be straightened under anaesthesia, the cast or caliper applied, and the patient allowed to walk with crutches. The shoe should be left off for 48 hours, because a pressure sore may develop on the

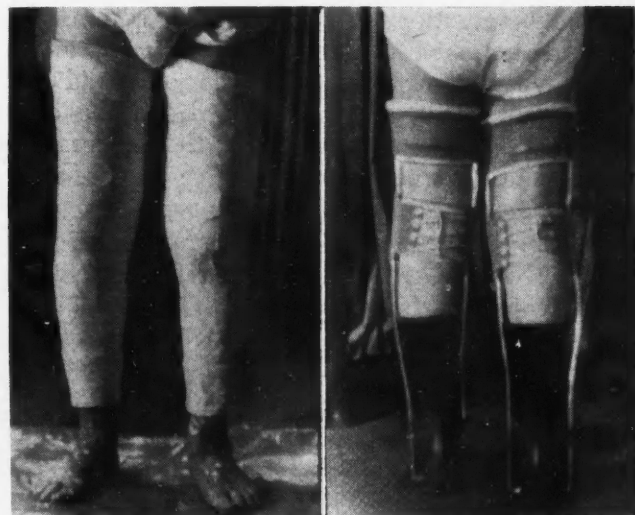


Fig. 5a

Fig. 5b

Fig. 5a.—Two painful knees: two plaster casts applied.
Fig. 5b.—Same patient later with two calipers replacing casts.

heel while the shortened flexors are being stretched. The lower leg is supported at the back by a padded plaster slab, and the lower ends of the caliper are kept apart with a wooden spreader. After 48 hours the shoe can be worn and the patient treated in the manner already described.

Swelling of the joint does not contraindicate the operation of forcible extension; there is no severe reaction if the manipulation is confined to one firm movement and the leg is fixed firmly in extension. All swelling subsides very soon. If it is a slight and recent deformity (within three years) and if the joint cartilage is intact, a good range of flexion will return when the caliper is removed. If the joint had been disorganized before, the operation is performed with the hope of achieving a stable ankylosis in extension. In many of these cases, however, a surprising amount of painless flexion returns (Fig. 6); it should not be actively sought.



Fig. 6.—Range of flexion two years after flexion deformity had been corrected under anaesthesia by this method.

Great force should never be used, for fragile bones may break and nerves and vessels may tear. A deformity too gross and too old cannot be treated in this manner. If it can be partly corrected, the leg may be fixed in its new position and the deformity fully corrected a few days later. Gradual correction by traction or by wedging of plasters has always failed because the patient has not been able to bear the prolonged drag on the posterior ligaments. Any procedures, moreover, which necessitate long-continued rest in bed are inadvisable. The patient is kept at his job, and other joints are not likely to become involved.

For several years, I used cylindrical plasters and allowed the patient to walk on the straight leg. But the band caliper is often superior because it avoids pressure sores and peroneal palsy, and it is superior to the ring caliper because it can be fitted without troublesome procedures in measuring.

TWO CURRENT FALLACIES

Many rheumatic patients suffer a great deal from two current fallacies:⁷ (1) the belief that they should put their painful joints through their full range of movement every day; (2) the fear that their joints will ankylose if they are completely immobilized for a few weeks.

The synovial membranes are inflamed and friable, and excessive movements intensify the inflammation. We should think of the function of each joint and try to preserve that. The knee is intended to bear weight, and the wrist is intended to be a stabilizer and a pivot for the hand. The arthritic knee does not need the 150 degrees of flexion which is sought so persistently. And the wrist does not need much flexion and extension so long as it can be rotated and the fist can be clenched. Plenty of exercise of the limb is necessary, but the damaged joint should be rested. When the splint has been taken off, the range of the joint will increase gradually so long as it is not forced.

Immobilization for three weeks seldom causes ankylosis of the knee if the cartilage is intact. Rather it increases the range, because the inflammatory process goes into reverse and pain and muscular spasm are reduced. When the cartilage has gone, ankylosis may occur in a good position, and the patient is extremely grateful.

REST VERSUS MOVEMENT

A few years ago Dr. N. Swanson¹⁰ of Toronto outlined a method of treatment of polyarthritis by continuous immobilization. The problem of rest versus movement has been debated from time to time since the days of John Hunter. Robert Bridges, the poet laureate, was one of the few who advocated splinting of rheumatic joints.² Hugh Owen Thomas¹¹ and his nephew Robert Jones⁵ showed clearly the value of fixation of diseased joints of all kinds. But this teaching was gradually forgotten as the urge to manipulate tempted successive generations of doctors. Phelps⁹ of New York showed that arthritic joints did not ankylose if they were immobilized; on the contrary, ankylosis was prevented by the suppression of the arthritic process.

At the Royal Society of Medicine in 1935, Kindersley⁸ of Bath pointed out how the arthritic joints were benefited by continuous fixation. Since then Tippet¹², Bell,¹ Duthie,³ Gariépy^{4a} and Swanson¹⁰ have shown that the fears of ankylosis are not well founded. One of the disadvantages of the method is the muscular wasting and weakness. If the patient is put to bed for the duration of the fixation, general weakness ensues. These difficulties can in large part be overcome if the patient is not put to bed but is encouraged to use the affected limb while the damaged joint is immobilized.

SUMMARY

In rheumatoid arthritis, it is supremely important that patients should be able to walk and to use their hands.

If flexion deformities of knees and wrists are prevented, arthritic patients will never become crippled.

Deformity of the knee can be prevented by keeping it extended in a caliper and encouraging the patient to walk.

Deformity of the wrist can be prevented by continuous immobilization in plaster splints which allow the fingers to be used and the hand to be rotated.

Arthritic joints which are immobilized for a few weeks do not ankylose.

REFERENCES

1. BELL, B. T.: *M. Clin. North America*, 24: 1735, 1940.
2. BRIDGES, R.: *St. Bart's Hosp. Rep.*, 12: 175, 1876.
3. DUTHIE, J. J. R.: *Practitioner*, 166: 22, 1951.
4. FICAT, P. AND ARLET, J.: *Rev. rhumat.*, 23: 17, 1956.
- 4a. GARIÉPY, R.: *Ann. Rheumat. Dis.*, 15: 268, 1956.
5. JONES, R.: *Brit. M. J.*, 2: 2, 1909.
6. KELLY, M.: *Acta rheumat. scandinav.*, 3: 203, 1957.
7. KELLY, M.: Active immobilization for rheumatoid arthritis, *Documenta Rheumatologica*, Basle, 1959.
8. KINDERSLEY, C. E. AND BURT, J. B.: *Proc. Roy. Soc. Med.*, 29: 237, 1936.
9. PHELPS, A. M.: *New York M. J.*, 51: 536, 1890.
10. SWANSON, N.: *Canad. M. A. J.*, 75: 257, 1956.
11. THOMAS, H. O.: Diseases of the hip, knee and ankle joints, H. K. Lewis & Co. Ltd., London, 1878.
12. TIPPETT, G. O.: *Brit. J. Rheumat.*, 2: 195, 1940.
13. VAINIO, K.: *Acta rheumat. scandinav.*, 4: 22, 1958.

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RÉSUMÉ

L'arthritique grabataire dans la plupart des cas est devenu impotent par déformation en flexion des genoux. Un cercle vicieux s'est établi ensuite puisque le repos au lit est désastreux pour les articulations, les os et les muscles. Les sujets atteints de polyarthrite chronique évolutive ne doivent donc s'aliter que pour des périodes aussi brèves que possible. Si les genoux sont immobilisés en flexion, l'auteur suggère de les étendre sous anesthésie et de les conserver en extension par l'application immédiate d'un appareil plâtré. Il faut se garder d'appliquer une force trop grande au cours de cette manœuvre dans la crainte de rompre les os devenus fragiles. On peut conserver le tonus des quadriceps par des exercices de contraction répétés plusieurs fois par jour. En cas de faiblesse de ces muscles il convient de les aider dans leur tâche par l'application de plâtres cylindriques.

Les poignets sont la principale source de douleurs dans la P.C.E. On ne doit pas permettre que ces articulations fléchissent en pronation; il faut au contraire les immobiliser en bonne position et laisser le pouce et les doigts libres. Cette immobilisation diminue beaucoup les douleurs dans les doigts.

L'immobilisation d'une articulation enflammée ne mène pas nécessairement à l'ankylose. Au contraire lorsque l'inflammation s'est calmée l'articulation gagne une plus grande mobilité. Le secret du succès est de ne pas forcer une articulation malade au delà du champ d'action que lui permet la lésion. Si le cartilage a été détruit, l'immobilisation dans un appareil plâtré permet à l'ankylose de s'établir dans la position la plus favorable et la plus utile.

Case Reports

PNEUMOCYSTIS CARINII PNEUMONIA*

REPORT OF A CASE DIAGNOSED DURING LIFE

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THERE HAS BEEN an increasing awareness of the interesting condition, pneumonia due to *Pneumocystis carinii*, in the past few years. There are possibly many instances of this disease hidden in autopsy files, and now that the condition is recognized as a clinical entity many more cases will doubtless be recognized in their true light.

The patient was an infant girl born October 6, 1958. Her first admission was to another hospital on October 31, 1958, at the age of 25 days, with a severe staphylococcal skin infection particularly affecting the abdominal wall, due to *Staphylococcus aureus*, coagulase positive, which was sensitive to chloramphenicol (Chloromycetin), erythromycin and oxytetracycline (Terramycin). This cleared up on local

application of neomycin ointment. During this admission a systolic murmur was noted which seemed to be maximal over the apex of the heart, but an electrocardiographic tracing was considered normal. At the time of discharge on November 14, she weighed 6 lb., having made no gain in the preceding 28 days. Her next admission to a second hospital was two weeks later. She then presented with vomiting, diarrhoea and skin pustules. This was treated with tetracycline (Achromycin) and penicillin. On the day before the present admission she had neck stiffness and irritability, but spinal fluid examination was negative. She was transferred to the Brandon General Hospital on December 9, at which time she had a severe staphylococcal skin infection.

Physical examination showed a slightly dehydrated pale, malnourished infant of about two months; weight 6 lb., temperature 104° F. The infant had a weak cry and lay with her head arched backwards. There were many pustules over the upper part of the trunk and several abscesses on the scalp, the largest measuring about 2.0 cm. in diameter.

On December 10, the large abscesses on the scalp were opened and drained, and culture yielded a profuse growth of *Staphylococcus aureus*, coagulase positive, sensitive to erythromycin and chloramphenicol. The white cell count at this time was 12,400 per c.mm. A diagnosis of staphylococcal pyoderma and malnutrition was made.

On treatment with hexachlorophene soap (pHisohex) and chlorhexidine (Hibitane) locally, and erythromycin

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systemically, the infant gradually improved. By December 28, the skin was clear, and the infant was discharged. At this time the weight was 7 lb. 7 oz.

Final admission.—The final admission was on January 30, 1959, at the age of four months. The mother stated that four days before this admission the infant had developed recurrence of skin infection with small pustules on the scalp. She was seen by her own doctor at home, where treatment was again instituted with erythromycin orally. Two days before admission the baby began to cough and run a low-grade fever, and for 24 hours before admission had been taking very little by mouth.

The local doctor when contacted stated that the home conditions were very poor and the mother apparently had not always carried out the treatment recommended. One of the siblings had been treated for rat bites, and the condition of the home was quite unsanitary.

Physical examination.—The patient was a very small, scrawny, sick-looking infant appearing to be one month of age but actually four months old. There was marked lack of subcutaneous fat but no loss of skin turgor or other evidence of dehydration. Many small pustules were seen on the scalp, two of these being approximately 1.0 cm. in diameter. No other skin lesions were present. The infant had marked buccal moniliasis. Respirations were rapid and shallow and the alæ nasi flared with each inspiration. No dullness could be noted in either lung field and there were no definite adventitious sounds. Some retraction of the lower costal margin was present on inspiration. No other significant abnormalities were noted. The weight was 7 lb. 15 oz. An admission diagnosis of staphylococcal pyoderma, possible staphylococcal pneumonia, thrush, and severe malnutrition was made. A radiograph of the chest was reported as follows: "The heart and great vessel shadows are not remarkable. The diaphragms are within normal limits. The lung fields appear clear." There was no evidence of any pleural effusion or pneumothorax.

A vein was cut down upon and a hypotonic multi-electrolyte infusion started. Intramuscular chloramphenicol (Chloromycetin) 100 mg. every four hours was started on admission.

On February 1, the child's condition had deteriorated. No physical signs of pneumonia were found, but respirations were grunty and rapid. A radiograph showed widespread pneumonia but no pneumothorax or empyema. The radiological report was as follows: "Re-examination of the chest shows some infiltration at the right base. Some less extensive peribronchial infiltration is also shown at the right apex. There is some quite dense consolidation of the left upper lobe. The right lower lobe appears generally clear. The findings are consistent with an extensive pneumonia. There has been marked deterioration in the appearance of the chest in the interval since the last examination 48 hours previously." By 3:45 p.m. on February 1, her condition was worse, with grey cyanosis. The chest was still clinically normal.

On February 2, at 11:00 a.m., there was not much change; some crepitations were present over the right base. The infant lay with her head retracted because of air hunger, but there was no neck stiffness.

On February 3, 11:00 a.m., the infant was deeply cyanotic, requiring continuous oxygen in a croupette. If the croupette was opened the infant became almost

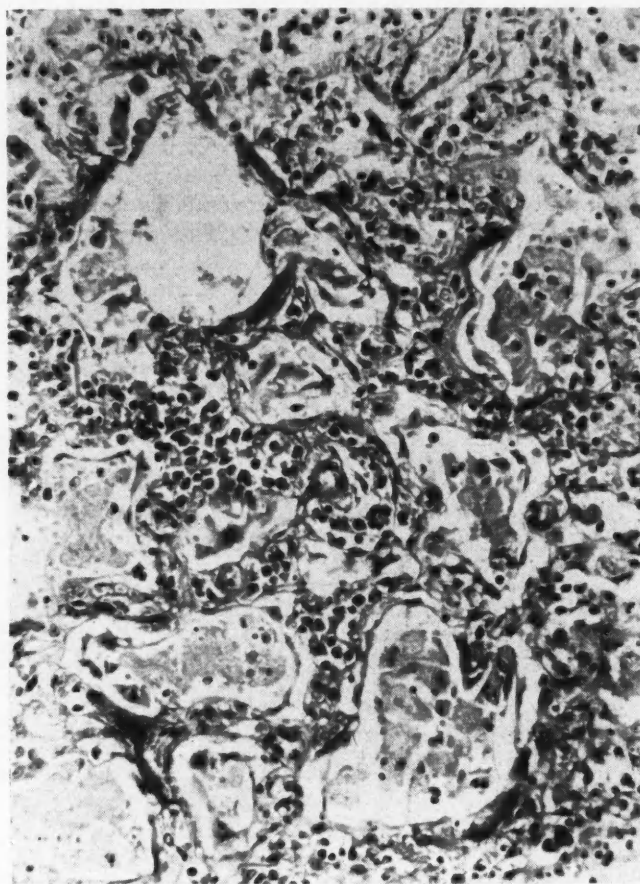


Fig. 1.—Histological section of lung showing interstitial infiltrate and alveolar exudate. Giemsa stain $\times 184$.

black. Occasional fine crepitations and rales were heard over the right base. A bedside radiograph taken at this time was reported as follows: "A single AP film of the chest was made on the ward with the portable equipment. This again shows the extensive consolidation involving the major part of the right lung and the left upper lobe. The left lower lobe still appears generally clear. The findings are again consistent with a widespread pneumonia."

Until this time it had been considered likely that the infant had a staphylococcal pneumonia. Because of the radiological appearance, the very marked cyanosis and air hunger associated with minimal, if any, local signs of pulmonary involvement, a diagnosis of *Pneumocystis carinii* pneumonia was now considered probable.

On February 4, the infant appeared slightly improved, although she was quite distended. The cyanosis did not appear quite as marked as on the previous day. On examination of the chest no adventitious sounds were heard. At 4:00 p.m. on February 4, the cyanosis suddenly became very marked, and the baby ceased to breathe.

Laboratory Examination

December 10, 1958. Hb. - 8.6 g. %. Hæmatocrit - 27%. M.C.H.C. - 31%. Leukocyte count - 12,400. Differential: Neutrophils - 66%. Lymphocytes - 30%. Band forms - 4%. Smear - essentially normal other than slight hypochromia.

January 31, 1959. Hb. - 11.8 g. %. Leukocyte count - 18,200. Unfortunately a differential count was not done at this time.

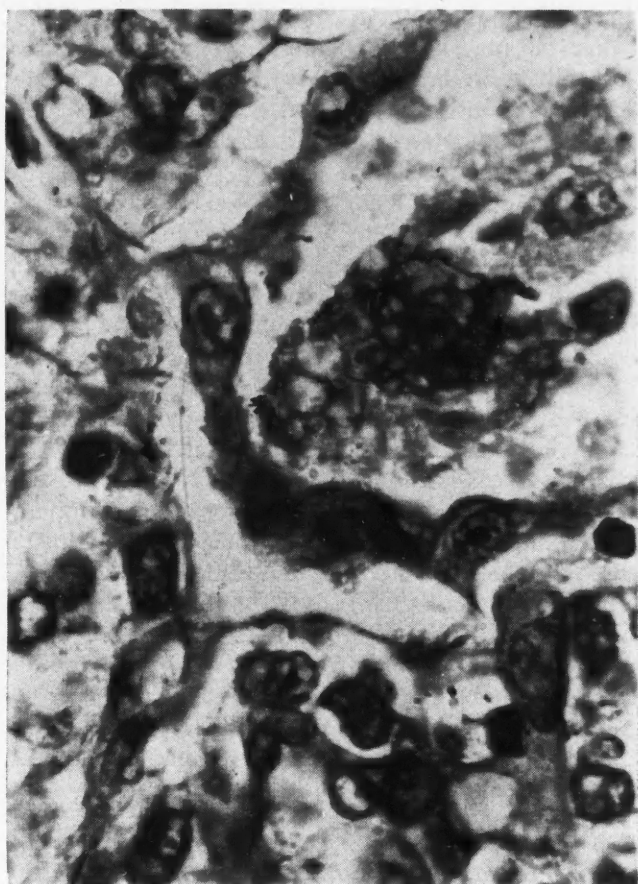


Fig. 2.—Histological section of lung showing typical foamy intra-alveolar exudate. Giemsa stain $\times 1150$.

Autopsy Findings

The body was that of an extremely pale infant girl, four months of age, weighing 7 lb. The anterior fontanelle was widely patent and somewhat depressed. There was cyanosis of the lips and nailbeds, and several pale, circular, old scars were present over the anterior aspect of the chest and abdomen. The abnormal gross findings were confined to the thoracic cavity. There was no free fluid, no pleural adhesions and no evidence of pneumothorax. The right lung weighed 110 g. and the left lung 90 g. The pleural surfaces were of a deep reddish-blue colour showing slight mottling. There were no subpleural hæmorrhages or petechiæ. Both lungs felt indurated throughout all lobes. The bronchi contained some muco-purulent material. On section the lungs cut with the consistency of liver and showed no obvious areas of aeration. The cut surfaces showed a mottled appearance, some areas being greyish in colour while others were dark red or bluish. The lungs had the appearance of hepatic tissue. The right side of the heart was slightly distended with blood clot. There was no ventricular hypertrophy and the heart weighed 35 g. No cardiac congenital abnormality was found.

Microscopic Findings

On routine hæmatoxylin and eosin sections, the lungs showed a striking picture (Fig. 1). There was little similarity to normal lung tissue and the main features were the interstitial infiltration and the material present in the alveoli. The alveolar interstitial infiltrate was exclusively mononuclear and consisted predominantly of lymphocytes and plasma cells. Many of the alveoli appeared completely collapsed by the dense

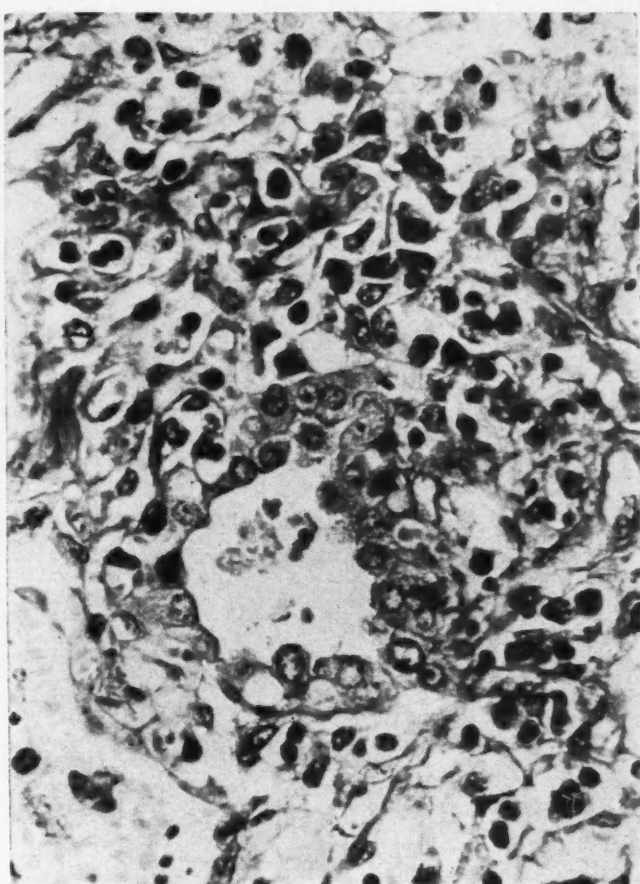


Fig. 3.—Histological section of lung showing alveolar lining hyperplasia. Giemsa stain $\times 460$.

interstitial infiltrate, while most of the others showed varying degrees of distortion and compression. For the most part the alveoli were filled with a slightly eosinophilic fibrin-like material among which were moderate numbers of mononuclear cells, foamy macrophages and alveolar lining cells. The typical honeycombed material was extremely scanty in this case when compared with previous illustrations of this disease (Fig. 2). Occasional alveoli showed marked hyperplasia of their lining cells (Fig. 3). With the Giemsa stain the honeycombing became more apparent, and the typical punctate or angular, darkly staining protozoa could be identified (Fig. 4). The lungs were markedly hyperæmic but there was no evidence of bronchopneumonia. The liver showed a moderate fatty metamorphosis and several areas of superficial ulceration of the oesophagus were present.

DISCUSSION

It is not proposed to give a comprehensive report of the literature or the many aspects of this disease since they have been fully covered in recent papers. Recently two papers appeared in the same issue of this journal. Berdnikoff¹ reviewed the Canadian picture, and with the further case reported by Junger and Wyllie² there would appear to be 25 cases reported in Canada. The first report of this condition appeared in the United Kingdom literature in 1955,³ and in the same year the first United States report was published,⁴ followed by the first Canadian paper.⁵

Pneumocystis carinii pneumonia has been recognized for some time in Europe and many cases have

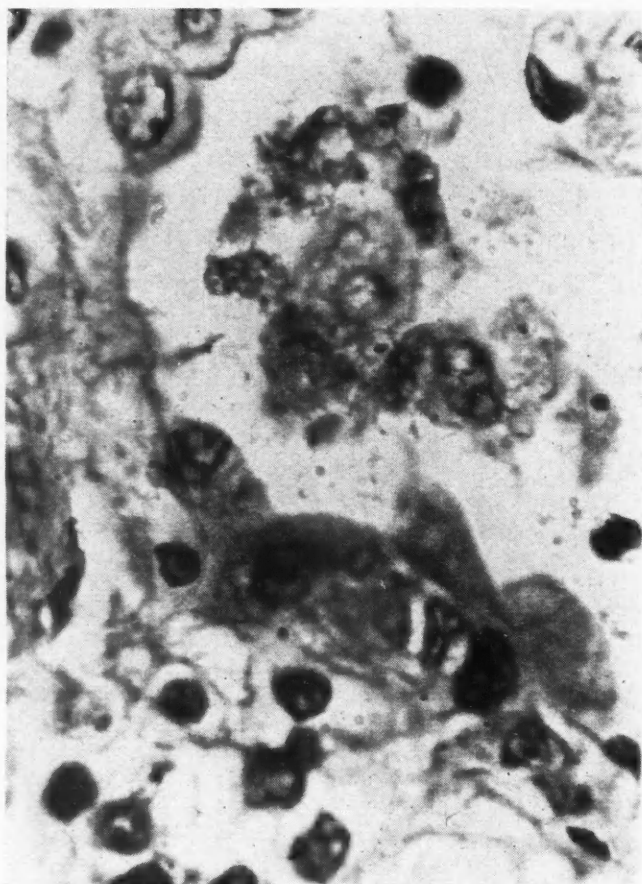


Fig. 4.—Histological section of lung showing alveolar "honeycombing" with scanty protozoa. Giemsa stain $\times 1150$.

been reported from Switzerland, Germany, Austria, Yugoslavia, Czechoslovakia, Hungary, Italy and Scandinavia. Gajdusek⁶ in a comprehensive review of the disease reports on his personal visit to a special isolation ward in Ljubljana, Yugoslavia, where 11 beds were set aside for infants with this disease. He reported that much of the time the ward was occupied, often full.

The etiological agent causing this disease is probably a protozoan parasite, although some consider it to be a fungus. The disease was first described in 1909 by Chagas in Brazil in the lungs of guinea pigs. Subsequently the organism has been found in the lungs of rabbits, rats, guinea pigs, dogs and monkeys.

The disease usually has its onset between the sixth and the sixteenth week of life, and has been reported in adults, usually associated with some chronic debilitating illness. The incubation period is thought to be about 40 days. The disease usually has a slow insidious onset, and tachypnoea and cyanosis of the lips and under the eyes may be the first indications of respiratory tract involvement. Physical findings are minimal and completely out of line with the degree of dyspnoea, sternal retraction, abdominal respirations, cyanosis and tachypnoea. Radiologically a diffuse ground-glass appearance with emphysema is the usual picture. Grossly the lungs are grey or greyish-pink and firm, and do not collapse when the chest is opened. Mediastinal emphysema or pneumothorax may be

found. The heart may be slightly enlarged but other organs show no significant changes. Histologically there is an extensive mononuclear cellular infiltration with a striking absence of polymorphonuclear leukocytes. This infiltration fills the alveolar septa. Plasma cells are usually prominent in this infiltration. The alveoli are often lined by large cuboidal epithelial cells which are sometimes found lying free in the alveolar lumina. The characteristic feature of the disease is the foamy honeycombed material present in the alveoli amongst which small compact masses, one or two microns in diameter, are seen. These small masses are sometimes difficult to identify in hæmatoxylin and eosin sections, but can readily be identified by special stains, in this particular case using Giemsa stain. The condition has been associated with hypo- or agammaglobulinæmia and with cytomegalic inclusion disease. The mortality is in the region of 20 to 25%.

The epidemiological aspect of the disease is still not clear. It has been suggested that the agent passes to the newborn from an inapparent infection of the mother's genital tract; however, airborne dissemination seems most likely. It is possible that the organism is a saprophyte in human lungs and only under certain debilitating conditions such as cytomegalic inclusion disease, malnutrition, prematurity or malignant neoplasm is the organism able to become clinically manifest. In the present case the vermin-infested home raises the possibility of a rat or dog being the source of infection.

Laboratory aids do not materially help in the diagnosis of this condition. Lung puncture would be pathognomonic, but it is unlikely that this procedure would be carried out very often. Retropharyngeal swabs have been suggested as a means of diagnosis, but culture of the parasite on media or in experimental animals has not yet been developed as a diagnostic tool. Skin testing and complement fixation have been used with variable success. Therapy is purely supportive, and as yet none of the many antibiotics, steroids or anti-protozoal agents have proved their value, although antifungal agents are worth a trial.

SUMMARY

A further case of *Pneumocystis carinii* pneumonia diagnosed during life is reported. This case would appear to be the twenty-sixth reported in Canada. Attention is drawn to the paucity of organisms seen, and the scanty alveolar "honeycombing", even though the other microscopical features and gross and clinical findings were typical of the condition.

Our thanks are due to Dr. Jan Hoogstraten, pathologist, The Children's Hospital, Winnipeg, for his interest in this case, and to Dr. J. Stratton, the family physician who referred the patient to this hospital.

REFERENCES

1. BERDNIKOFF, G.: *Canad. M. A. J.*, 80: 1, 1959.
2. JUNGER, P. W. AND WYLLIE, J.: *Canad. M. A. J.*, 80: 35, 1959.
3. BAAR, H. S.: *J. Clin. Path.*, 8: 19, 1955.
4. LUNSETH, J. H. *et al.*: *J. Pediat.*, 46: 137, 1955.
5. GAGNÉ, F. AND HOULD, F.: *Canad. M. A. J.*, 74: 620, 1956.
6. GAJDUSEK, D. C.: *Pediatrics*, 19: 543, 1957.

DIAGNOSIS OF ENDOMETRIAL CARCINOMA IN SITU BY SUCTION DILATATION OF THE CERVIX UTERI

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IN THE last four years over 200 dilatations of the cervix for diagnostic purposes have been performed at the Ottawa General Hospital using perforated Hegar dilators to which vacuum suction is applied.^{1, 2} Continuous vacuum suction during dilatation of the cervix prevents intrauterine increased hydraulic pressure which can spread infection, viable endometrium and carcinomatous cells through lymphatics, blood vessels and Fallopian tubes. It was believed in the past that solid Hegar dilators spread the disease which we seek to diagnose. The specimen bottle added to the apparatus has proven useful only occasionally. The diagnostic value of this technique is demonstrated in the following case.

Mrs. B.L., a white woman now 52 years old, had her first dilatation and curettage performed for abnormal uterine bleeding in April 1955. The histopathological examination was reported as showing "active and rather disorderly inflammatory epidermization with proliferative and papillary changes". An endocervical biopsy performed on June 25, 1957, was negative. Dilatation and curettage using vacuum suction was performed in July 1957 because of postmenopausal bleeding. This produced no endometrial tissue on curettage but material found in the suction bottle and examined in the pathology department of the Ottawa General Hospital was reported as showing "endometrial carcinoma" (Figs. 1 and 2). After total abdominal hysterectomy and bilateral salpingo-oophorectomy, multiple sections of the uterus showed no residual carcinoma. It must be noted that in this case the Papanicolaou smear obtained on June 25, 1957, was

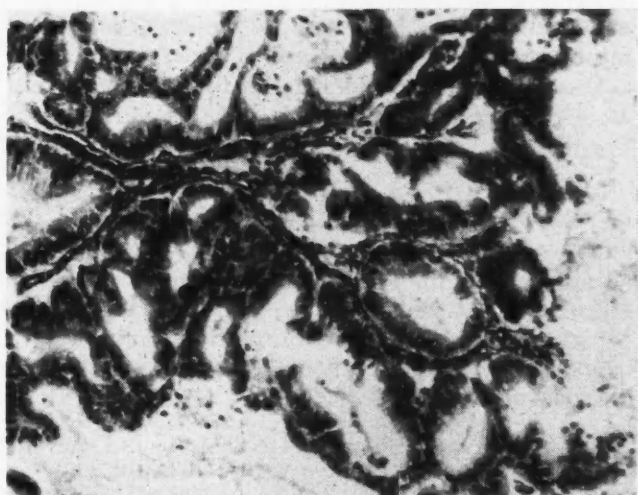


Fig. 1.—Section of endometrial tissue obtained by suction dilatation showing adenocarcinoma of the uterus. (H. and E. stain, $\times 200$.)

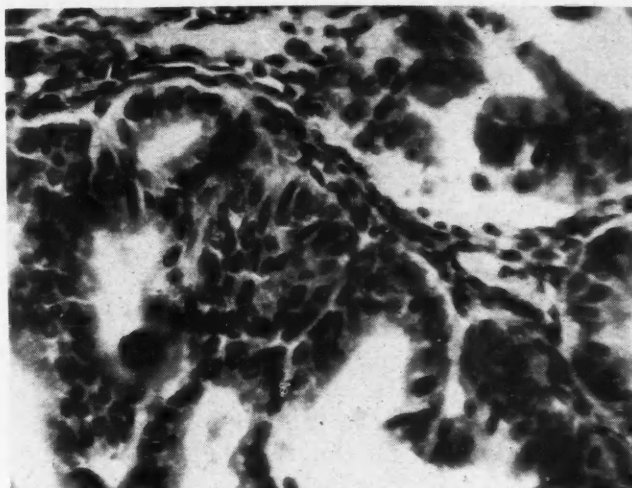


Fig. 2.—Same section as in Fig. 1, magnification $\times 400$. The dark round spot in both pictures is an artefact.

interpreted as resembling "a menopausal picture class I.A. normal". The previous specimens in this case were reviewed and the case was discussed at the Ottawa General Hospital surgical-pathological conference of July 25, 1957. It was generally agreed that this was an early carcinoma of the endometrium *in situ*. Two years later the patient is healthy and asymptomatic; the Papanicolaou smears are negative.

Carcinoma *in situ* is a malignant condition in which the only abnormalities are morphological changes in the cells themselves and in their arrangement in the tissue. There is no evidence of infiltration. It is now generally accepted that in nearly all cases at this stage the malignant process is fully established and that progression to malignancy with invasion and metastasis is only a matter of time. The cure rate of proven cases should be 100%. The histopathological diagnosis is usually not easy, since extreme degrees of atypical proliferation are common. Novak³ and Hertig and Sommers⁴ point out that it is impossible to define with certainty the borderline between atypical hyperplasia and malignancy.

SUMMARY

Suction dilatation technique of the cervix uteri, frequently used at the Ottawa General Hospital during the last four years, enabled us to demonstrate a case of carcinoma *in situ* of the endometrium which would otherwise have been missed by two curettages and routine Papanicolaou smears. The concept of carcinoma *in situ* of the endometrium is discussed briefly.

I am indebted to Dr. A. Hurtig for permission to report this case.

REFERENCES

1. HURTIG, A.: *Canad. M. A. J.*, 74: 64, 1956.
2. HURTIG, A.: *J. Obst. & Gynec. Brit. Emp.*, 63: 725, 1956.
3. NOVAK, E. AND NOVAK, E. R.: *Gynecologic and obstetric pathology*, 4th ed., W. B. Saunders Company, Philadelphia, 1958, pp. 162 and 236.
4. HERTIG, A. T. AND SOMMERS, S. C.: *Cancer*, 2: 946, 1949.

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LIVER INJURY INVOLVING RIGHT HEPATIC ARTERY LIGATION, COMPLICATED BY SURVIVAL

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ON THE evening of December 1, 1958, a 26-year-old previously healthy lay brother of a seminary was crushed against some wooden posts of a corral by a bull. He was able to extricate himself by climbing the fence and was then given aid and brought in to the Notre Dame Hospital, North Battleford.

Examination on admission revealed signs of intra-abdominal bleeding, though no fractures were detected nor was there any significant fall in blood pressure. Along with resuscitative measures laparotomy was performed. At operation there was evident intraperitoneal bleeding, and a large split was found in the right lobe of the liver extending up through the central tendon of the diaphragm and the parietal pericardium. The damage was repaired by sutures, but to control the bleeding from the right lobe of the liver ligation of the right hepatic artery was found to be necessary. Retrospectively, we consider that it was a mistake then not to insert drains, the abdomen being closed by interrupted sutures.

The immediate postoperative course was stormy and the patient remembers little of day-to-day events. Signs and symptoms of ileus and bile peritonitis came on slowly, associated with a fall in haemoglobin value to 11.55 g. per 100 ml., and a rise of serum bilirubin level to 3.3 mg. per 100 ml. and urea to 56 mg. %. Intravenous therapy maintained kidney function adequately.

A second laparotomy was performed on December 17, 1958. Six litres of bile-stained ascitic fluid was suctioned off and a general plastic peritonitis noted. Dilated and twisted loops of small intestine were disentangled and a Miller-Abbott tube was threaded into the duodenum. Penrose drains were now placed in the pouch of Morison and in the pelvis. At this time the right lobe of the liver appeared pale and somewhat green, but liver biopsy was not deemed suitable. In view of the considerable remaining distension, the abdomen was closed with interrupted tantalum wire sutures.

During the next two months his condition remained perilous. Weight loss continued and amounted to over 28 lb. Feeding was never satisfactory nor did his bowels function normally. Even with enemas, urecholine and pitressin, colonic function was minimal. Serum bilirubin level rose to 8.6 mg. % and then fell to 1.4 mg. %. Anaemia persisted and the white cell count fluctuated. The total proteins varied between 4.8 and 6.6 g. % with an almost equal albumin to globulin

ratio. These figures were affected by day-to-day therapy with blood, serum albumin, and electrolyte solutions.

Shortly after the second laparotomy, signs developed of pus beneath the left leaf of the diaphragm, associated with a sterile left pleural effusion up to the second interspace, pericarditis, and atelectasis of the right lower lobe. In view of his critical condition the abscess was needled and aspirated through the 9th intercostal space posteriorly in the mid-scapular line. Two aspirations over five days produced 400 c.c. of creamy pus which grew a pseudomonas, slightly sensitive to polymyxin E only. Aerosporin was given in a daily dose of 100 mg. intravenously for nine days. At final laparotomy little evidence of this abscess was seen. The signs of sub-diaphragmatic abscess resolved and a tender mass developed in the hypogastrium and left iliac fossa. This mass disappeared after passage of a large quantity of purulent urine. Only after this event did his bowels start to move spontaneously and oral intake of food increase.

Toward the middle of February, vomiting and jaundice recurred along with leukocytosis, pyrexia, and pain and tenderness in the right hypochondrium. Haemoglobin value 11.2 g. %; bilirubin 5.50 mg. %; total proteins 7.0 g. %; albumin 3.6, globulin 3.4 g. %. A third, and we trust final, laparotomy was undertaken on February 18, 1959; large inflammatory lymph nodes obstructing the common bile duct were noted in the porta hepatis, and an abscess in the right paracolic gutter was found and drained. Cholecystotomy was also performed. At this time a biopsy of the right lobe of the liver showed regeneration of hepatic cells with inflammatory changes in portal triads; a portion of liver tissue showed gross destruction, scarring and small areas of necrosis. Hereafter convalescence was uneventful and sustained. Appetite increased, and by discharge on April 30, 1959, he had gained 24 lb. At this time the blood picture and protein and bilirubin values were normal. A previous bromsulphalein test had shown 27% retention at 30 minutes, and this was now 5%.

We remain astounded at the fortitude and faith of our patient through five months of varying misfortune.

SUMMARY

The purpose of this short clinical description, unencumbered by the minutiae of day-to-day events, is to record an instance of liver injury in which right hepatic artery ligation was performed to control haemorrhage; and to outline the major events during recovery and convalescence.

All of us are intensely grateful to the patient's family and his order for their constant support, and to the Sisters of Charity of Providence and the entire nursing staff of the Notre Dame Hospital for their unswerving help. We thank Dr. W. H. Houston for the pathology reports.

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Special Article

OLD CROW—A HEALTHY INDIAN COMMUNITY*

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LAURENCE IRVING,[‡] Anchorage, Alaska

IN THE COURSE of investigations on physiological response to cold, a field study of Arctic Indians was undertaken at the village of Old Crow, Yukon Territory, for six weeks from August 20 to October 1, 1958. In addition to the physiological studies,¹ observations were also made on the state of health of the community as a background for their adaptation to their Arctic environment. These observations form the basis of this report.

Old Crow was selected by one of us (L.I.) as a suitable place to carry out the physiological studies after a previous visit there for biological reconnaissance, partly because of the apparent good health and the social organization of the village. The impression of good health has been borne out by detailed health examination of most members of the village. Although the village was selected for these very reasons and, therefore, may not be representative of Indian villages, the fact that it seemed to be unusually healthy led us to make further enquiries into the social and economic background of the population in an attempt to gain some insight into the reasons for their well-being.

GEOGRAPHY AND HISTORY

Old Crow is situated where the river of that name enters the Porcupine, a large northern tributary of the Yukon (Fig. 1). It is 35 miles east of the Alaskan boundary, about 100 miles north of the Arctic Circle and about the same distance inland from the Arctic coast. The elevation is approximately 900 feet above sea level. At its eastern end the Porcupine Valley is separated from the Mackenzie Valley by the Richardson Mountains. McDougall Pass, between the headwaters of the Rat River draining into the Mackenzie and the Bell River draining into the Yukon, crosses the mountains at an elevation of about 1200 feet. Although McDougall Pass is shorter, the overland winter route between Fort McPherson and La Pierre's House on the Bell River was the main route used by the Hudson's Bay Company when the area was first opened up to the fur trade.² This trade route into Alaska has now been bypassed, leaving the Porcupine Valley little disturbed by outside communication. The freight route to Old Crow from Canada is now by river

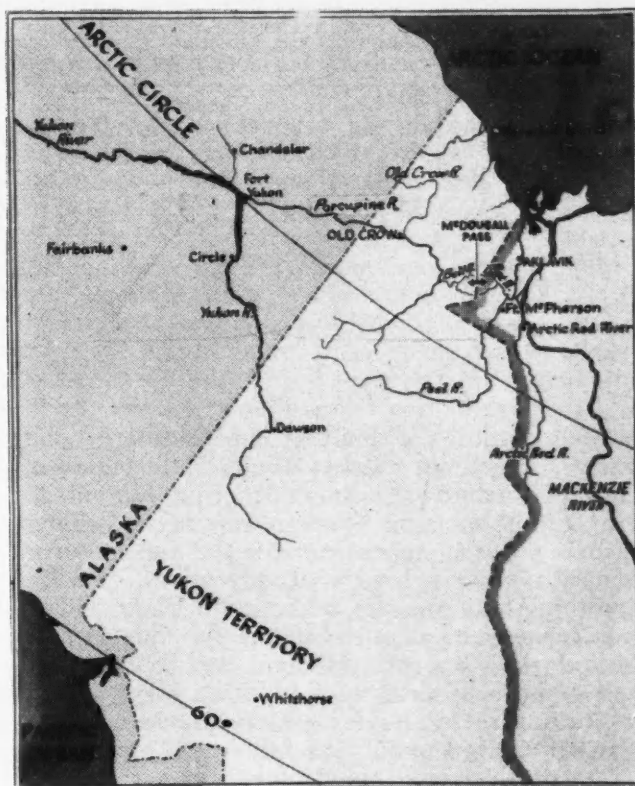


Fig. 1

barge down the Yukon from Dawson into Alaska and up the Porcupine. Light aircraft reach Old Crow easily either from the Mackenzie Valley or from Fort Yukon, Alaska. The area is underlaid with permafrost but the valleys and lower slopes of the hills are covered with spruce forest which reaches its limit about 50 miles to the north.

The present population are Athapaskan Indians of the Kutchin tribe who have always lived in that region.³ Different bands speaking a closely related language inhabited the regions of the Upper Porcupine and the Peel River to the east and south-east, the wide valley of the Old Crow River to the north and the Yukon in the region of Fort Yukon, Alaska, to the south-west.⁴ The Hudson's Bay Company early established a trading post at Fort Yukon but, as this subsequently became United States territory, the post was moved back up the Porcupine, first to Old Rampart and later to New Rampart House on the Alaskan boundary. The post was abandoned by the Hudson's Bay Company in 1893 but the village remained there until 1912, when the settlement was moved to the present location.⁵ Before that time, small groups of families were often scattered up and down the Porcupine and Old Crow Rivers but since then the population has become concentrated. The establishment of a Royal Canadian Mounted Police post, the Anglican mission and a school has encouraged this trend. The Catholic mission was established about seven years ago. There has been a succession of independent traders since the Hudson's Bay Company left the area; at present there are two local traders, one Indian and one white.

The independence of the family group is still respected within the village organization, and people still move about within their wide territory

*Resulting from an expedition for physiological studies in Arctic adaptation by a group of American, Norwegian, British and Canadian scientists based on the Arctic Health Research Center, Anchorage, and with the aid of a grant from the National Science Foundation of the United States to the University of Alaska.

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TABLE I.—POPULATION OF OLD CROW, YUKON TERRITORY

	No.	%
Pre-school children	39	23
School children 5-14 years	45	27
Young adults, 15-34 years	36	22
Males	20	
Females	16	
Adults, 35 years and over	47	28
Males	21	
Females	26	
Total at present in village	167	100
Away from village:		
In hospital	3	
At school	4	
Working	7	

for the purpose of hunting and fishing. Lone families, sometimes even a woman with children, may spend months at a time away from the village in favourable spots for hunting, trapping or fishing. Caribou and some moose provide the major source of meat. This is somewhat precarious, as the migratory routes of the animals fluctuate. Other fur-bearing animals are hunted for their pelts. Muskrat skins are the principal export and most families move up into the Crow Flats every spring for "ratting". Dog teams which provide winter transport are fed mainly on fish which are netted and trapped during the summer and fall. The spruce forest provides for housing and fuel. Both men and women, even into old age, live lives of strenuous physical activity in this Arctic climate.

POPULATION

The present population of Old Crow is approximately 170. Their distribution by broad age groups is shown in Table I. In addition there are eight white residents: a detachment of two R.C.M.P. officers, three clergy, a registered nurse who is the wife of the Anglican missionary, a trader and an elderly prospector who has lived there for many years.

GENEALOGY

The genealogy of the village was recorded on the basis of family histories, usually cross-checked from more than one source. As English is a common language even amongst the elders, the danger inherent in using interpreters was negligible. Use was also made of the parish records of the Anglican mission and the vital statistics records maintained by the R.C.M.P. As the people seemed prepared to discuss parentage in a matter-of-fact way without the degree of reticence often attached to this subject, the genealogies worked out on a clinical basis are considered to be probably accurate. However, blood samples were also taken from the population of school age and above, for determination of blood group substances. These studies, which will be reported in detail elsewhere,⁶ confirmed the clinical findings. Table II shows the distribution of the population based on the clinical

TABLE II.—INDIAN POPULATION OF OLD CROW BY RACE

	Full-blood Indian	Part-white	Half-white	Unknown
Number	117	36	12	1
Per cent.	70.5	21.7	7.2	0.6

assessment. It is seen that 70% of the population are pure-blood Indian. Many of the Indian family trees can be traced back three or four generations. The 21% who are listed as part-white are the offspring of the people making up the 7% who are half-white, as most of the white admixture was at least two generations ago.

Although these northern Indians are neighbours of the Arctic Coastal Eskimos, there is no evidence from their blood groups of racial admixture between them.⁶ The native names for birds give another interesting illustration of the independence of the Indians and Eskimos. Out of 91 Indian and Eskimo names for the same birds, only two show resemblance, whereas a high proportion of common birds are similarly named by Alaskan and Greenland Eskimos.⁷ Aside from the white admixture, the Indians at Old Crow are homogeneous not only in their genetic and cultural background but also in their way of life. The present social organization of the village is described later.

MEDICAL ARRANGEMENTS

The Indian and Northern Health Service maintains a registered nurse in the village. The incumbent is the wife of the Anglican missionary. Drugs and other medical supplies come up by barge but can also be obtained by aircraft from Aklavik, with which the R.C.M.P. maintain daily radio contact. Patients requiring hospital care are flown out by chartered aircraft to Aklavik, which is about one and one-half hours' flying time to the east. X-ray surveys are done annually and the films are read and kept at Aklavik. The medical officers at Aklavik, who have hospital and surgical facilities there, visit the village and see the patients referred to them by the nurse. An ophthalmologist, with Aklavik as temporary headquarters, visited Old Crow this spring and not only examined eyes and prescribed glasses but had facilities for eye operations. Although a dentist stationed at Aklavik was scheduled to visit Old Crow, the visit has not been made for some years. The R.C.M.P. have dental instruments for extractions and for temporary fillings. Some villagers visiting at Fort Yukon in Alaska have received medical advice and hospital care there.

By prior arrangement with the Indian and Northern Health Service the medical facilities of the expedition were put at the disposal of the nurse. Several cases were seen and recommendations for treatment or evacuation made during the six weeks' stay; several teeth were also pulled.

MEDICAL EXAMINATIONS

Most of the young adult males were medically screened to assess them as subjects for the physiological experiments. This included a medical history, physical examination and the measurement of height, weight and skin-fold thickness from which the lean body mass was calculated. One of us (R.W.) is currently engaged in a study of arteriosclerotic heart disease in Alaskan natives. Therefore, both males and females over 34 years were also examined with particular reference to the cardio-respiratory system. This examination included 10-lead ECG records and serum sampling

TABLE III.—EXAMINATION OF CHILDREN

School children—total	45
Moderate or grossly enlarged tonsils	10
Chronic otitis media:	
scarred drums only	6
active disease	2
Dental caries, moderate or severe	11
Healed tuberculous adenitis	1

for cholesterol determination. All the school-children and many of the pre-school children, particularly those whose health the nurse held in some question, were examined by one of us (H.W.) with special training and experience in paediatrics.

Blood was drawn from almost all the population of five years and over. As mentioned above, red cells were preserved in Alsever's solution for identification of blood groups by Miss Marion Lewis and Dr. Bruce Chown in their laboratory at Winnipeg. The serum was separated and kept for subsequent study of blood lipids, proteins and antibodies. These findings will be reported at some later date. In a few cases with clinical indications blood was also taken for anti-streptolysin titre and for protein-bound iodine determination.

RESULTS OF MEDICAL EXAMINATION

Seventeen young men of the village were examined as potential subjects. One had had a below-knee amputation of one leg as a boy and wore a prosthesis (which he made himself by copying the one with which he had been provided originally), and one had limitation of exercise tolerance, a mild scoliosis and evidence of pleural thickening resulting from old pulmonary tuberculosis. The others were all in very good health, although two had scars of healed tuberculous cervical adenitis and six had had mumps in the spring of this year. The average calculated lean body mass for the nine Indians who were used as experimental subjects was 55 kg. or 86% of total body weight compared to 57 kg. or 78% for the whites, indicating that they are less fat than the white subjects. Clinically they are slender and well-muscled. The average height of these subjects was 67 inches (1.68 m.).

The main defects found in the examination of the school children are listed in Table III. One of the children had clinical signs of hypothyroidism but she had been previously "outside" for investigation and was on treatment. The thyroid dosage was probably inadequate, as the blood level of protein-bound iodine was 3.2 μ g. per 100 ml. (borderline euthyroid-hypothyroid). Four children had heart murmurs of questionable significance. Blood for anti-streptolysin titre estimation was taken from them; values were all less than 100 Todd units and, therefore, do not suggest active rheumatic carditis. In addition, a three-year-old infant with a history of chronic chest infection and failure to thrive and who had finger clubbing was diagnosed as a case of mucoviscidosis. It was recommended that she be evacuated south for investigation and treatment. The carious teeth cause considerable pain and disability. The University of Manitoba School of Dentistry have indicated an interest in collaborating with the health authorities to give dental care as part of a research

project on genetic and dietary factors in dental health in such isolated northern populations.

The adults of 35 and over were principally examined for evidence of arteriosclerotic heart disease. Of 46 examined, 10 gave a history of old tuberculosis and some of these had scars in the neck due to old adenitis. One woman is paraplegic and has been so for several years, probably owing to multiple sclerosis, and one woman with a chronic ulcerating lesion about the nipple was recommended for evacuation for biopsy and treatment. In one thin but active man the question of hyperthyroidism was raised, but the blood level of protein-bound iodine was normal. Although one elderly man had a cardiac arrhythmia, no cases with clear-cut arteriosclerotic heart disease were seen.

The results of these examinations may be summarized as follows. General nutrition was considered to be good; there was no evidence of specific deficiencies of vitamins or minerals; obesity was rare; there was no evidence of metabolic disease and no cases of arteriosclerotic heart disease were discovered. Although there were many scars of healed tuberculous adenitis and a history amongst a fair number of the population of having been in hospital for tuberculosis, recent x-ray surveys as well as our clinical examinations show no evidence of active tuberculous disease at the present time. In support of this there are very few cases with corneal scars resembling phlyctenular keratoconjunctivitis. In the few that do exist there is usually a history of trauma. Grossly enlarged tonsils and middle ear disease were present in some of the children, as were carious teeth, but both of these were less than is usually found in comparable populations in Alaska and the eastern Arctic. The strenuous physical activity, even of the elderly, the cold exposure and their relatively low economic status have not had an apparent deleterious effect on health.

DIET

Although the major source of protein and fat comes from caribou hunting and from fishing, none of the population lives on a pure animal diet. This is supplemented by the purchase of cereals, coarse and refined carbohydrates, dried and sometimes fresh fruits and vegetables, canned goods and dried milk imported from the outside by the traders. Local berries are gathered by the women and are eaten in the fresh state or preserved.

Although a proper dietary survey could not be undertaken, one female member in each of six families was asked to keep a meal-by-meal record of the family for eight days. Two of the families were widows with children; three were small families of four and five each, two of which were considered to be well-off; and the last one was reasonably well-off but included ten children. The following impressions were gained from a study of these records: animal protein in the form of fresh or dried meat or fish was usually eaten twice and often three times a day; the children drank milk once a day or more often; cereal in the form of bannock, rice, pancakes or bread formed part of almost every meal, often together with refined

TABLE IV.—ESTIMATED ANNUAL CASH REVENUE AND EXPENDITURES

Revenue	
(1) Estimated annual income from the sale of furs, based on the year ending February 1958.	\$22,000
(2) Estimated annual income from family allowance, old age pension, relief and sale of wood.	18,000
Total.	\$40,000
Expenditures	
(1) Food stuffs, flour, cereals, milk, butter, sugar, canned goods, etc.	\$20,000
(2) Clothing, ammunition, fish nets, etc.	10,000
Total.	\$30,000

carbohydrate in the form of syrup or jam; fruit, either dried, fresh or canned, was used frequently but vegetables were used only occasionally.

Therefore, although meat is an important item of diet even in the poor families, the well-to-do families also take a considerable proportion of their total calories as cereals or refined carbohydrate. The proportion of calories derived from fat is difficult to assess. Total caloric intake is not in excess of requirements, for no one examined was really obese. The extensive use of milk, all of which is imported, probably results from health education in the school and by the resident nurse.

The Indians estimate that a large family requires 100 caribou a year. It is difficult to assess how much of the meat is wasted through spoilage. Any spoiled meat is not entirely wasted but is used for the dogs, which usually are fed on dried fish or dried muskrat.

Alcoholic beverages cannot be consumed legally by the Indians and there are few infractions of this law. Whites and part-Indians who have "white status" may legally bring in spirits for their own use. However, little alcohol appears to be used by any group in the community.

ECONOMICS

In order to import food and other commodities the community must have a source of revenue. This comes from the sale of furs, principally muskrat, from the sale of wood and from family allowance and old age pensions. Some of the members of the community find temporary or seasonal jobs in Alaska or in the Mackenzie delta. A rough estimate of the annual revenue and how it is spent was worked out with a local merchant (Table IV). This narrowly based economy means that in time of caribou scarcity government relief is necessary. Although the fields in which such peoples may be gainfully employed by using their special skills are limited, they have not been fully developed. One which comes to mind is wild life conservation. The adaptation of Arctic natives to their environment is associated with extensive information about that environment. These skills, which have been used and acknowledged by scientists,⁷ are important potential assets for conservation.

CLOTHING

For the most part the clothing used is imported. However, some articles of local design and manu-

facture are used in summer and particularly in winter. In the summer, moccasins are universally worn. These are made of smoke-tanned moose and caribou leather decorated with beads and trimmed with fur. In the wintertime, mitts of the same materials are used and heavier footwear is necessary. Caribou skin is sometimes used for outer winter clothing, and it is widely used for bedding.

The processing of hides by the women is an intricate one involving scraping, drying, treatment with "caribou brain water" and smoking. Various combinations are used to achieve different products. Although no measurements were made, the smoke-tanned moose hide used for gloves and moccasins appears to have good insulating and vapour permeability properties and is quite pliable.

HOUSING, WATER SUPPLY, WASTE DISPOSAL

The log houses are sturdy one-storey structures, generally built directly on the ground to save heat. The food caches are built up on piles. A few of the inhabitants use tents on tent frames both summer and winter. Most of the wood stoves in use are of local manufacture by the old white prospector from oil drums. These are considerably cheaper and more suitable than imported stoves.

Water is carried by bucket from the river during the summer, and river ice is used in winter. There is, of course, no treatment of the water supply. However, there are no communities upstream.

Although the permafrost is only a foot below the surface, the pit latrine is the method used for human waste disposal. The soil is light and the village is kept drained of surface water by ditches. Village regulations, usually followed, require dumping of other waste in pits or on river ice in winter, and the village area is usually clean and tidy.

The dogs are usually kept tethered below the river bank on the village outskirts or behind the village, although puppies are allowed to stray in the village. All dogs are immunized against rabies by the R.C.M.P. The caribou are known to have visceral cysts, and dogs are not fed raw entrails. The incidence of infestation with *tænia* (cysticercosis) in the dog population would be an interesting index of the success of these measures.

SOCIAL ORGANIZATION

The police, who provide the services of law and order, and the church, which gives religious guidance and schooling, are respected agencies who also provide leadership and advice in many community activities. However, they wisely encourage a large measure of local autonomy. There is a tradition of strong local government by an elected chief and councillors. The present chief has recently been elected. Three ex-chiefs, whose rule extended over a period of almost 40 years, still live in the village and are active and vigorous in local affairs. Family bonds are strong and the women are also active in community affairs, both as individuals and through the women's auxiliary of the church.

This social organization not only sustains an orderly and friendly society but initiates and gives direction to plans for the present and future well-being of the community. The leaders of the com-

munity are cognizant of the transitions that must come with more frequent and closer contact with the outside and hope that they will be prepared to meet these changes.

The organization of the Old Crow Ski Club is an example of such progressive thinking. One of the Catholic priests is a competent skier and, although the difficulties seemed insurmountable, the community organized and supported the clearing of trails, the procurement of equipment and the training of the youngsters, as well as actively participating in the sport. A team of young skiers competed last winter at Fairbanks, Alaska, and acquitted themselves well. A letter from a member of the ski club committee to the Fairbanks papers clearly showed how highly they prize this sort of contact between their boys and girls and the outside world as a means of preparing them for a broader life while retaining the pride and dignity of their own culture.

The native cultural activities and entertainments include skill in hunting and physical fitness for the men, and the tanning of hides and bead work for the females. Dancing is popular with all ages, even the children. The occasion of a successful hunt for moose is taken to have a feast in which the whole community shares. Oratory is popular with the adults, which is in keeping with their tradition of democratic local government.

CONCLUSIONS

Old Crow differs somewhat from many other Indian or Eskimo communities, although there may be other remote villages like it. It appears to be healthier than the average, and better organized and more vigorous than most. The factors involved are probably multiple; its contact with whites has not been a sudden one; they may have been fortunate in that the white people there are in remarkably good accord with each other and show their sympathy, understanding and respect for

the Indians; they may have been much more fortunate than other communities in their own successive leaders. Whatever the factors involved, the difference between this and other communities seems worthy of study in the hope that, while the community by further contact gains the cultural and material benefits enjoyed by the rest of the country, they may retain, through their special skills, the ability to make contributions to our society, perhaps first in the field of sports, perhaps even in politics. Their potential in the field of conservation has been mentioned, although to be developed to the point where they could be used for something more than manual labour would require special training and perhaps more formal education than they now have available.

It seems to us that this or similar villages offer opportunities to study positive factors of health; health agencies often consider only disease. Consideration should also be given to making use of the village for further physiological studies while it retains its homogeneity both genetically and in the manner of living. Apart from matters of health and physiological studies in such communities, it seems also evident that retention of racial and cultural homogeneity is not incompatible with progress.

The measure of the debt to our colleagues and to all the inhabitants of Old Crow, which we gratefully acknowledge, is obvious from the nature of this paper. We are also indebted to Dr. H. I. Drever, University of St. Andrews, and to Mr. Alan Cook for helpful comments.

REFERENCES

1. IRVING, L. *et al.*: Unpublished data.
2. STEFANSSON, V.: *North West to Fortune*, Duell, Sloan & Pearce Inc., New York, 1958.
3. JENNESS, D.: *The Indians of Canada*, 4th ed., Queen's Printer, Ottawa, 1958.
4. OSGOOD, C. B.: *Contributions to the ethnography of the Kutchin*, Yale University Press, New Haven, 1936.
5. Unknown author: *A short history of Old Crow, R.C.M.P. Files*, Old Crow, Yukon Territory.
6. LEWIS, M., CHOWN, B. AND HILDES, J. A.: Unpublished data.
7. IRVING, L.: *Arctic*, 11: 117, 1958.

CANADIAN JOURNAL OF SURGERY

The contents list of the October 1959 issue of the *Canadian Journal of Surgery* (No. 1, Vol. 3) is as follows:

History of Canadian Surgery: Ingersoll Olmsted (1864-1937). A. I. Olmsted.

Original Articles: Observations on thrombosis and endothelial repair following application of external pressure to a vein. H. Rocke Robertson, J. R. Moore and W. A. Mersereau; Polyps of the rectum and colon in children; a ten year review at the Hospital for Sick Children, Toronto. A. S. Mallam and S. A. Thomson; The use of an isolated ileal loop for total replacement of the ureter. T. K. Goodhand *et al.*; Ileocystoplasty. A: Experimental studies on electrolyte behaviour. W. K. Kerr, A. G. Keresteci and V. N. Kyle; Hépatolobectomie droite. R. Cauchon, P. Brochu and L. Levasseur; Intussusception in infants and children. C. W. Clark, R. H. Watson and H. W. Johnson; Description d'une nouvelle technique chirurgicale de suspension artificielle des organes intra-pelviens. J. Y.

McGraw and E. Samson; Traumatic dislocation of the hip; a follow-up study. K. S. Morton; Teflon fabric for ligament reconstruction: an experimental study. J. Gort and O. Rostrup; Experimental studies on the production of deep hypothermia by means of a pump oxygenator and heat exchanger with a note on the clinical application. R. O. Heimbecker, W. E. Young and D. C. Sanford; Malignant duodenocolic fistula. B. M. Lefebvre and C. McG. Gardner.

Case Reports: Malignant duodenocolic fistula: report of a case treated successfully by mass resection. R. M. Janes and J. R. F. Mills; Evolution d'un cas de résection intestinale massive. J. Couture, G. Nadeau and R. Tourigny; Migration lente d'un corps étranger enclavé dans l'oesophage. J. A. Gravel, P. Painchaud and P. L'Espérance; A foreign body in the appendix: a report of an unusual case. M. H. W. Friedman and W. C. MacKenzie.

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A WEEKLY EVENT

Almost five years ago, the *Canadian Medical Association Journal* departed from a very long tradition and began to appear twice a month instead of monthly. This decision was taken after careful thought and with some trepidation by the Executive Committee and General Council of the Association because they regarded it as a logical step in the development of Canadian medical publishing. As events have turned out, any fears as to the success of the venture were unfounded, for the support given to this Journal by contributors, readers and advertisers in the last five years has fully justified the greater frequency of publication.

Having in mind the continued phenomenal growth of medicine in this country, the governing body of the Association this year decided to take the next logical step, and to arrange for weekly publication of the *Canadian Medical Association Journal* from the beginning of January next. This step will bring the Journal into line with practice in the United States, the United Kingdom, Australia, Germany, and some other countries. Those who hold up their hands in horror at the thought of more reading matter appearing in their mail each week may be consoled with the thought that there is no intention of eventually running a daily medical newspaper, though our French colleagues have tightened the schedule to twice a week. They may also be consoled with the fact that it is not intended to double the number of reading pages. Some additional space will be provided, in order to take the strain off present efforts to accommodate everything worthy of publication, but the main object of the exercise is to give members of the Association and other readers information at more frequent intervals. The publication will appear each Saturday, beginning January 2, 1960. We look for continued support from contributors, readers and advertisers and are confident that this step forward will be justified by future events.

Before deciding on this weekly publication, your Association had considered making alternative pro-

visions for inclusion of Canadian work by adding to the C.M.A. family of publications. Careful inquiry however failed to elicit any official or large-scale demands for such periodicals, and there was of course the ever-present danger in a country of this size of diluting good-quality papers with lesser material just to fill out pages.

As we look around at our weekly contemporaries, we notice that clinical investigators find these a convenient medium for the reasonably rapid publication of new material. It is hoped that the weekly appearance of the *Canadian Medical Association Journal* may stimulate investigators in Canada to offer more of the results of their investigations to this Journal than they have done in the past. With weekly publication, it should be possible to reduce the time lag for urgent material to a minimum. In addition, we must not forget that this Journal is the major voice of organized medicine in Canada. We hope that the weekly publication will enable members of this Association and its affiliated organizations to keep more closely in touch with the affairs of their representatives and with those trends in the practice of medicine which fall outside the scope of science. It has been suggested as a fault of general medical journals such as this that they try to be all things to all men. Yet this is an accusation which might equally well be levied at any world-famous daily newspaper. And just as the integrating and unifying influence of a good newspaper is needed by a stable community, so the integrating and unifying influence of a general medical journal appears to us to be needed more than ever in this day and age. The new weekly will therefore attempt to present to its readers, as this Journal has done in the past, a picture of the whole of Canadian medicine as it develops, and of the main trends in medicine outside our boundaries.

Editorial Comments

SAFE DRIVING

The fact that the week December 1 to 7 has been designated "Safe Driving Week" reminds us once more of the gaps in our knowledge of automobile accidents. This was dealt with in a panel discussion which the Canadian Highway Safety Conference had called on Medical Aspects of Traffic Accidents, and which took place in Toronto last May. At this panel discussion, Dr. Milton Brown said that accidents are among the chief causes of death. They now number 220,000 per year in Canada and cause 3000 deaths and 78,000 injuries. No less than 200,000 years of "working life" are lost each year, and this figure is much greater than that due to either heart disease or cancer.

At this panel discussion, several points were raised. One concerned the securing of the co-operation of the public in reduction of automobile accidents. There is no doubt that the apathy of the

public in this respect contrasts sharply with the horror and interest aroused by, say, an aircraft disaster. In addition, the general attitude of the public to driving is basically incorrect; driving an automobile is not a basic right but a privilege granted to those who have shown themselves capable of controlling their vehicle on the road. Because of this, as Dr. Tillman pointed out in the discussion, the doctor is placed in an awkward position when he is expected to pronounce on fitness or unfitness to drive. If the public could be educated to the understanding that loss of a licence is not a punitive action but done for the protection of the driver and others on the highway, law enforcement might be easier.

It is difficult for the physician to say whether an individual is physically fit to drive or not. Unless uniform standards can be set up—based on more research—physicians will have to make arbitrary decisions. Moreover, as Dr. Dewar mentioned in discussion, it is by no means certain that many accidents can be prevented simply by taking physically unfit drivers off the road. Available data suggest that the majority of accidents are caused by "normal" people. People harbouring destructive feelings or anxiety should be given a way out other than by working out their feelings by staging an automobile accident. Another field for research concerns the "warning signals" which make a driver aware of a reduction in his capacity to drive.

However, the apparent complexity of the problem need not deter us from action. The Ontario Department of Transport, for example, has set up an advisory board to deal with the question of research into automobile accidents, while the Canadian Medical Association through its national, provincial and local committees is studying the medical aspects of traffic accidents. These bodies find themselves in a situation very common in medicine. Prevention always tends to lag behind therapy, and there is nothing peculiar about the great contrast between the highly efficient ambulance services and surgical services available to the victims of accidents and the comparatively unrewarding efforts at prophylaxis. An intensive effort such as will be put forth during the week of December 1 to 7, to acquaint the public with such facts as are known about the subject must undoubtedly yield some results. If we waited until we knew everything about a medical subject before we took action, we would still be in the dark ages.

SPLINTING IN RHEUMATOID ARTHRITIS

Splinting is an old modality for the prevention and correction of deformity in rheumatoid arthritis, which has of recent years received new attention. Goldthwaithe and his group, at the Robert Breck Brigham Hospital in Boston, were probably the originators of the modern principles of application of splints. Dr. Michael Kelly¹ of Melbourne, whose article appears in this issue, names some of the many authorities who have since then developed different techniques of splint application. It is now realized that not only can deformity be

largely prevented, but also the disease process may be modified with adequate splinting. A correctly fitted, comfortable splint, maintained in position for some time, not only allows pain and therefore deforming spasm to subside but also sets the stage for the reversal of the inflammatory process. The dangers of ankylosis from such temporary immobilization are usually greatly exaggerated, as pointed out by Kelly,¹ Duthie² and Swanson.³

By splinting in a functional position, muscle atrophy due to an improper position need not arise, particularly if adequate physiotherapy is prescribed too. The initial period of continuous immobilization is followed by one of intermittent immobilization, a descriptive phrase first used by Taylor.⁴ The length of time and manner in which a limb should be immobilized depends on the state of activity of the joint disease. If there is fluid in the joint, it may safely be continuously immobilized for three to four weeks. Indeed, Duthie² recommends longer. Should the joint be "a dry" one, this period may be too long and fibrous adhesions are likely to appear after two weeks.

Kelly rightly stresses the important concept of maintaining function during treatment, particularly in the knees and hands, as walking and self-care respectively depend upon preservation of these joints. Rest alone is not enough. Not only must there be properly controlled rest (correct posture in bed and adequate splinting) but physiotherapy, particularly muscle-building exercises, preceded perhaps by heat to relieve pain and spasm, should be prescribed right from the start.

Kelly also has interesting views on manipulation. In Canada at any rate, few rheumatologists would feel that a rheumatoid joint should be manipulated. There are, however, those elsewhere who do advocate manipulation, among them Harris⁵ of the Royal Devonshire Hospital, Buxton, who claims very successful results. While it is possible that more manipulation should be tried, it should be surely an unusual necessity, since by use of the splinting measures Kelly himself outlines, the activity in most joints will subside, with consequent straightening. Manipulation might be desirable when all activity has ceased, and only soft tissue contracture prevents full extension. The procedure is not without danger, as blood vessels and nerves may rupture, with consequent paralysis and paresthesia, and even death from fat embolism has taken place. Osteoporosis is an obvious contraindication, and as this is generally present in bones surrounding a rheumatoid joint sufficiently diseased to be ankylosed, this is a further reason for caution in advocating manipulation.

While the principles of splinting have been recognized for many years, the custom of applying them is more "honoured in the breach than the observance". This may be chiefly because of the inconvenience of a physician having to ask an orthopaedic surgeon to make a splint or the mess that the physician himself must make, if he uses plaster. Hence, the search for newer, better materials, such as plastics. This Journal⁶ was the first to describe such a new plastic, DuraFoam, which is the nearest to the ideal available today. Because of its remouldability at temperatures

easily borne by the body, its use in situations described by Dr. Kelly, for serially straightening the limb, is obvious. Some plastics, such as fibre-glass, require a positive mould which is time-consuming and expensive to make. Other plastics that can be moulded directly to the skin usually do not fit adequately and are less useful than Dura-Foam.

It is encouraging to realize that, on the other side of the world, principles for treatment of arthritis, similar to those practised here, are believed in. Dr. Kelly is to be congratulated on drawing attention to the prevention of deformity at a time when the Canadian Arthritis and Rheumatism Society is planning further measures for the rehabilitation of the crippled arthritic patient.

"The opportunity to emancipate himself from the needless consequences of disability should be the right and reasonable expectation of every disabled Canadian."⁷ J. N. SWANSON

REFERENCES

1. KELLY, M.: *Canad. M. A. J.*, 81: 827, 1959.
2. DUTHIE, J. J. R.: *Practitioner*, 166: 22, 1951.
3. SWANSON, N.: *Canad. M. A. J.*, 75: 257, 1956.
4. TAYLOR, D.: Medical exhibits and lectures. Personal communication.
5. HARRIS, R.: Personal communication.
6. SWANSON, N.: *Canad. M. A. J.*, 79: 638, 1958.
7. DUNLOP, E.: Rehabilitation for the disabled in Canada, Canadian Arthritis and Rheumatism Society, Toronto, 1958, p. 6.

BREAST FEEDING

The superiority of breast feeding over bottle feeding is almost undisputed, and yet the majority of infants on the North American continent are denied this advantage. Salber, Stitt and Babbott,¹ however, reporting the breast feeding patterns of women attending the family health clinic in Boston, deduce a welcome revival of interest in breast feeding. It is evident that present-day bottle feeding methods have reached a high standard of simplicity and reliability. Furthermore, the growth of artificially fed infants as judged by conventional standards appears adequate. The bottle-fed infant, nevertheless, is confronted by certain hazards, some immediate and tangible and others remote and speculative.

The greater solute load of cows' milk (some five or six times that of human milk) may jeopardize the water reserves in a young infant, so increasing the risk of hypernatraemia, now found in as many as 25% of cases of infantile gastroenteritis.² The excess calcium content of cows' milk and the cavalier use of vitamin D increases the likelihood of "supermineralization" and may contribute to the recently noted incidence of the hypercalcaemia syndrome of infants.³ Infantile scurvy, currently showing a disquietening increase in certain parts of Canada,⁴ is altogether a disease of the artificially fed infant. In rural areas, the use of well-water containing nitrate in excess of 10 parts per million in the preparation of infant formulas may result in a puzzling and occasionally fatal form of cyanosis due to methaemoglobinemia.⁵ The recent controversy concerning optimal protein requirements

for infants⁶ highlights the superiority of human milk protein, at the same time acknowledging this superiority as a nutritional mystery.⁷ The long-term effects of cows' milk feeding have not been studied and some have expressed concern about the complacent assumption that rapid growth in mass of a young infant fed cows' milk necessarily represents optimal growth.⁸

The emotional deprivation occasioned infant and mother by the substitution of a bottle for the intimacy of the breast must surely be an aggravation to our already anxiety-prone society. The sour, cheesy unpleasant smell of the baby fed cows' milk cannot enhance the mother-infant relationship. These and other often stated reasons should commend breast feeding alike to mother and physician. The study of breast-feeding patterns of 114 healthy, intelligent primiparae by Salber, Stitt and Babbott therefore makes interesting commentary. It is probably no revelation to most that 40% of the mothers decided not even to attempt breast feeding. The remaining 60% who put their babies to the breast achieved only indifferent success. In fact, the incidence of secure breast feeding could not be established, so early and prevalent was the practice of mixed feeding. This goes far, most would agree, to defeating the advantages of breast feeding. The findings, although disappointing, represent an improvement on the trend reported by Meyer from his survey of 2¼ million births in the United States in 1956.⁹ The mothers studied by Salber and her colleagues were not, however, a representative group. Many were the wives of college students and most of the families were in a low-income bracket and lived under circumstances of serious economic stress.

A number of variables were examined for their influence on breast feeding. These included the mother's age, birthplace, ethnic group, religion and education as well as her "expressed attitude toward breast feeding" and her previous experience in child care. The father's education and social status were also considered. It was found that an expressed wish to breast feed on the part of the mother, together with a superior education and elevated social status, favoured breast feeding. The other variables were of little or no significance. The greater incidence of breast feeding among well-educated women married to men of the upper and middle social class was considered by Salber and her associates as showing evidence of a returning interest in breast feeding, the members of these classes being, in their opinion, the first to be influenced by modes of infant feeding. It is also probable that within this group there prevails a more enlightened attitude towards the breast as a lactational rather than a sexual structure. The reasons given for not even attempting breast feeding were often multiple. The commonest was an "emotional barrier"; some mothers considered breast feeding too burdensome and many were dissuaded by the advice and example of their friends and relatives. The reasons most frequently given for weaning, once breast feeding had been started, were abnormality of the breast or nipple, unwillingness to continue feeding and insufficiency of milk, either actual or fancied.

The "emotional barrier" which discourages a mother from breast feeding or from continuing it when once begun requires further examination. The young mother-to-be is soon aware from the experience of those about her that breast feeding is essentially unreliable. Her medical attendant, from his own experience, is not likely to encourage any other belief. Breast feeding, although a natural function, is evidently not easily achieved for the majority. This is likely related to the tensions and anxieties so much a part of modern living which disturb in particular the expulsion or "let down" phase of breast feeding. This mechanism provides that milk secreted and accumulated in the breast is delivered to the infant.

A better understanding of the biology of lactation can reform this unhappy contingency. Waller,¹⁰ for example, reported that of 100 primiparae in his care, 83 were wholly and successfully breast-feeding six months after delivery. He advocated and practised: (1) pre-natal expression of the breasts as a means of providing free flow of milk down the ducts; (2) prevention of high tension or engorgement within the breasts by manual expression and the judicious use of oestrogens (high tension within the secreting alveoli is known to have an ill effect on later milk production); (3) support of the expulsion or "let down" phase of nursing by an appreciation of its mechanism and in particular its vulnerability to emotional factors. The care and attention devoted by Waller and his staff to the "nursing couple" appears to be unattainable in our present-day practice of obstetrics and paediatrics.

The discovery of an effective galactagogue which would safely ensure a free flow of breast milk might provide a desirable compromise and restore some of the lost confidence in breast feeding. The time-consuming breast expression which many women find tedious, uncomfortable and often beyond the scope of their manual skill could thus be eliminated. There are promising signs from dairy research that such a substance will yet be found. It is already known that unfractionated extracts of ox anterior pituitary raise the bovine lactational curve above that expected.¹¹ It is believed that the active principle is somatotrophin. Thyroid-active materials, such as iodinated casein and l-thyroxine, have been successfully used in dairy practice to increase milk yield.¹² The "let down" or "draught" reflex, which is evidently a function of the posterior pituitary, is being intensively studied,¹³ and means to its promotion may provide the key to successful breast feeding for many.

In the meantime, a better appreciation of the complex character of breast feeding is essential if it is not to continue to decline and become the province only of the "natural nurser" (a mother who takes it for granted that she will breast feed and succeeds with little or no instruction). A moment's thought will indicate how deplorably little time is devoted to the mechanism and management of breast feeding in the medical student's present curriculum. The field of human lactation as a research area must not be neglected, and studies such as those of Salber, Stitt and Babbott are indeed welcome signs of activity.

D. GREWAR

REFERENCES

1. SALBER, E. J., STITT, P. G. AND BABBOTT, J. G.: *New England J. Med.*, 259: 707, 1958; 260: 310, 1959.
2. FINBERG, L. AND HARRISON, H. E.: *Pediatrics*, 16: 1, 1955.
3. BONGIOVANNI, A. M., EBERLEIN, W. R. AND JONES, I. T.: *New England J. Med.*, 257: 951, 1957.
4. GREWAR, D.: *Canad. M. A. J.*, 78: 675, 1958.
5. MEDOVY, H.: *Ibid.*, 62: 228, 1950.
6. GORDON, H. H. AND GANZON, A. F.: *J. Pediat.*, 54: 503, 1959.
7. JEANS, P. C.: *Am. J. Dis. Child.*, 80: 363, 1950.
8. MAY, C. D.: *Pediatrics*, 23: 384, 1959.
9. MEYER, H. F.: *Ibid.*, 22: 116, 1958.
10. WALLER, H.: *Brit. M. Bull.*, 5: 181, 1947.
11. FOLLEY, S. J.: The use of hormones in nutrition: some practical possibilities, In: Present problems in nutrition research, symposium, Basel, 1952, edited by F. Verzar, *Experientia supplementum 1*, Verlag Birkhäuser, Basel, 1953, p. 214.
12. YOUNG, F. G.: *Brit. M. Bull.*, 5: 155, 1947.
13. HARRIS, G. W.: *Proc. Roy. Soc., Lond.*, ser. B., 149: 336, 1958.

DO ALKALIS CAUSE GASTRIC ACID REBOUND?

Several generations of physicians were told that the administration of alkalis produces a stimulating effect on the gastric secretion of acid, the so-called "acid rebound". Pereira-Lima and Hollander¹ have reviewed the literature on this subject since 1888. Analyzing the reports, based on investigations in human beings, the writers conclude that many of the older studies were probably unreliable and that more recent experiments have failed to confirm the rebound phenomenon, even in patients who showed hypersecretion in response to a histamine test performed on other days. Recent re-examination of this problem in animal experiments has also failed to furnish uniform evidence of rebound reaction to ingestion of alkalis. Pereira-Lima and Hollander conclude that there is no agreement in the literature concerning the existence of "acid rebound". There is also difference of opinion about the reason for such rebound, if it exists at all, and about the circumstances in which it would be produced. In their own experiments, which are reported in a paper following the one quoted, fasting Heidenhain-pouch dogs were given NaHCO_3 solutions in 1% and 2% concentrations and no acid rebound was obtained.

This critique of the apparently well-established and generally accepted phenomena makes one wonder how many other so-called "well-established facts" in gastroenterological physiology and pathology need revising. The remarks made by Davenport may be recalled in this connection. In reflecting on gastric secretion, he has clearly shown the number of things we still do not know about its mechanism and even about the major components of gastric juice. Gastrin is identical with histamine in Chicago and with polypeptide or a small protein in Montreal and Stockholm.² He mentions that we do not even know whether the pepsin of the gastric juice is actually the same as the pepsin so familiar to our chemists; even gastric mucus is still to some extent mysterious. It is encouraging to know that old-established statements are being subjected to critical analysis and revision is forthcoming. The day may not be too far removed when the mystery of peptic ulcer will cease.

W. GROBIN

REFERENCES

1. PEREIRA-LIMA, J. AND HOLLANDER, F.: *Gastroenterology*, 37: 145, 1959.
2. DAVENPORT, H. W.: *Ibid.*, 33: 15, 1957.

Medical News in brief

CARCINOMA OF THE PROSTATE

The comparatively high incidence of occult carcinoma of the prostate in elderly men is now well documented. In a recent paper, Butler and his colleagues of Cincinnati (*A.M.A. Arch. Path.*, 68: 243, 1959) describe a study of large tissue sections from 220 prostate glands obtained at necropsy from men over 50 years of age and without any clinical evidence of prostatic cancer. In each case, a single section of the entire prostate gland in the coronal plane was studied histologically. Of the 220 glands examined, seven showed an unsuspected carcinoma on naked-eye examination. Of the remaining 213 glands 64 contained one or more foci of carcinoma when surveyed microscopically. Hence the overall incidence of clinically occult carcinoma in this series is 32.2%. Of the 71 prostates in which carcinomata were identified, 40 had a single focus while 26 had more than one, and five had diffuse invasion of the whole gland.

The authors note that in their series 89% of carcinomas affected the lateral lobe and only 33.3% the posterior; this is at variance with the usual statement that most prostatic carcinomas arise posteriorly. This observation should reduce the sense of security conveyed to the physician by the absence of nodulation or induration on rectal examination or absence of positive findings on needle biopsy of the posterior portions.

Of 27 glands examined histochemically for enzymatic activity, six were found to contain a carcinoma.

PARALYTIC DISEASE RESEMBLING POLIOMYELITIS

Various virus diseases can cause poliomyelitis-like clinical pictures with and without paralysis. Rossi, Rench and Krech of Berne (Switzerland) discuss the various diseases caused by viruses and stress that they were able to confirm the presence of the virus of poliomyelitis only in two children out of seven with acute infections associated with paralysis. In addition to the better-known paralytic diseases due to virus encephalitis, infectious mononucleosis can be associated with paralysis. A third form, that of encephalomyelitis myalgica epidemica (Akureyri disease or Iceland disease, benign myalgic encephalitis), was first described by Gsell in military personnel and has been seen from time to time by others in Switzerland. Epidemic parotitis is another cause, and several epidemics with paralysis, including one in Russia, were found to be due to Cocksackie A virus. Examples of Echo virus and adenovirus producing infection with paresis are also reported.

In a discussion following this paper (*Schweiz. med. Wchnschr.*, 89: 688, 1959), one speaker mentioned that in 1959, isolation of virus, mostly from stools, resulted in the finding in 6% of poliomyelitis and in 94% of Echo and Cocksackie virus. The question of poliomyelitis-like disease occurring in populations which have been vaccinated against poliomyelitis is becoming more acute, as new viruses appear to take over in frequency in causing paralytic disorders.

A POTENTIAL HAZARD OF MODERN ANÆSTHESIA

The effort to minimize homeostatic disturbance during surgical intervention may result in administration of inadequate amounts of anæsthetic to the patient for analgesia and amnesia. With the use of neuromuscular blocking agents, this situation is more likely to occur as the patient is unable to give evidence of insufficient anæsthesia, and the signs used in the past to indicate this are not dependable. Cass and Phillips of Baltimore report such a case in a 40-year-old woman who underwent operation for vaginal hysterectomy and anterior and posterior colporrhaphy (*J.A.M.A.*, 170: 2069, 1959). Anæsthesia was induced with intravenous administration of thiopental, and the patient was given a continuous intravenous infusion containing 0.1% lidocaine and 0.025% succinylcholine.

Although the operation progressed uneventfully and anæsthesia was apparently smooth, the patient related later to the surgeon and anæsthesiologist that she had been intermittently conscious and unconscious during the three-hour anæsthetic period. She was able to tell of several incidents that happened during the operation and complained of having experienced severe, unbearable pelvic and perineal pain. The authors believe it quite possible that if she had been given an opiate preoperatively, they might have prevented this unpleasant experience (it was not given because of the known sensitivity of the patient to opiates). The interpretation of the signs of anæsthesia when using the newer anæsthetic agents and methods, and especially with the administration of neuromuscular blocking agents, needs special attention. The possibility that sufficient depth of anæsthesia has not been achieved must be kept in mind.

POSITIVE CYTOLOGY AND NORMAL CERVIX

With the increasing use of cervical and vaginal cytological studies, the problem arises of the management of that group of patients who have positive findings on cytological examination but no grossly visible lesion on the cervix.

Ferguson and Offen (*J.A.M.A.*, 170: 1892, 1959) find that one-seventh of their patients with positive findings fall in this group. Their practice is to call these patients back to the clinic as soon as possible and perform quadrant punch biopsies. An endocervical biopsy and endometrial biopsy are sometimes done at the same time. If these are negative for malignancy, and cervicitis is the only disease reported, the patient is simply observed once a month when smears are taken. This is carried on for six months and then once every three months for the next six months. After this the authors revert to the recommended annual cytological examination.

If at any time a positive smear is again noted, a cone biopsy and fractional curettage are performed. They add that, owing to an increasing awareness that carcinoma of the cervix may begin in the endocervical canal beyond the reach of the punch forceps rather than at the mucocutaneous junction, they find that they frequently perform a cone biopsy at once in women who have positive cytological findings but a cervix which appears perfectly normal.

VANCOMYCIN IN SEVERE STAPHYLOCOCCAL INFECTIONS

Numerous strains of *Staph. pyogenes* have almost invariably been found to be sensitive to vancomycin, an antibiotic developed in 1956. Dutton and Elmes of the Postgraduate Medical School, Hammersmith, England (*Brit. M. J.*, 1: 1144, 1959), report the treatment with vancomycin of nine extremely ill patients, three of whom were moribund when treatment was started. All except one had previously failed to respond to other therapy, and vancomycin saved the lives of five patients and controlled the staphylococcal infection in two others who later succumbed to infection with *Ps. pyocyanea*. Toxic effects consisted of thrombophlebitis and nerve deafness. The former can be largely prevented if vancomycin, which has to be given intravenously, is diluted in 250 ml. of saline or 5% glucose. Nerve deafness is particularly frequent in patients who have renal failure.

(Continued on advertising page 66)

NEW DRUGS

This listing of new products is based on information received from Dean F. N. Hughes, Faculty of Pharmacy, University of Toronto, and the *Canadian Pharmaceutical Journal*, to whom we owe thanks.

HORMONES

Methyltestosterone plus oestrogens: FOR-MATRIX (Pr), Ayerst

Description.—Each tablet contains: conjugated oestrogens equine (Premarin) 1.25 mg., methyltestosterone 10 mg., ascorbic acid 400 mg.

Indications.—Prevention and treatment of: postmenopausal osteoporosis, osteoporosis due to immobilization or to malnutrition, corticosteroid osteoporosis.

Administration.—One tablet daily, 21-day courses with a week's rest between courses. In the male the prostate gland should be checked when therapy is over long periods.

How supplied.—60.

Dexamethasone: POLANIL (Pr), Schering

Description.—Each tablet contains: 0.25 mg. dexamethasone (Deronil), 2 mg. dextrochlorpheniramine maleate (Polaramine), and 75 mg. ascorbic acid.

Indications.—Severe allergic and inflammatory disorders.

How supplied.—30 and 100.

6:21 Dimethyl ethisterone: SECROSTERON (Pr), B.D.H.

Description.—Orally active pregestational agent. Each 5 mg. tablet contains 5 mg. of Dimethisterone (6:21 dimethyl ethisterone), which appears to be more than 11 times as potent as ethisterone.

Indications.—Habitual and threatened abortion, sterility (due to endometrial dysfunction), menorrhagia, metrorrhagia, secondary amenorrhoea, premenstrual tension and toxæmia of pregnancy.

Side effects.—When given in recommended dosage Secrosteron manifests no side effects. Overdosage may produce pelvic pain resembling dysmenorrhoea and "fullness of the head" and dizziness.

Administration.—Orally 5 to 15 mg. daily. For most indications one tablet three times daily.

How supplied.—30.

ANTIMICROBIAL AGENTS

Sulfadiazine: OVOQUINOL (Pr), Nadeau

Description.—Each cone contains: di-iodohydroxyquinoline U.S.P. 75 mg., sulfadiazine U.S.P. 390 mg., phenoxy-ethanol B.P.C. 0.04 c.c., sodium propionate 500 mg., in a soluble base with lactose, dextrose and phosphate buffer.

Indications.—For the treatment of vaginitis and leukorrhoea.

Administration.—As prescribed by the physician.

How supplied.—Bottles of 15 and 100 cones. Also *Ovoquinol-Cestro*: same formula as above but with ethinyl-œstradiol, 0.01 mg. per cone.

Sulfadimethoxine: MADRIBON (Pr), Roche

Description.—Each drop provides 12.5 mg. 2,4-dimethoxy-6-sulfanilamido-1,3-diazine. One c.c. = approx. 20 drops. A well-tolerated sulfonamide with broad antibacterial spectrum and prolonged action.

Indications.—Respiratory, urinary, systemic and local infections due to susceptible micro-organisms.

Administration.—Initially: 250 mg./20 lb. body weight. Every 24 hours: 125 mg./20 lb. body weight.

How supplied.—Plastic dropper-bottles, 10 c.c.

Sulfadimethoxine: MADRICIDIN (Pr), Roche

Description.—Each capsule contains: Madribon 125 mg., thephorin 10 mg., N-acetyl-p-aminophenol 120 mg., caffeine 30 mg.

Indications.—Palliation of the common cold; prevention and treatment of secondary bacterial infections.

Administration.—Adults, first day, 2 capsules q.i.d.; 1 capsule q.i.d. thereafter. Children, first day, 2 capsules per 20 lb./body weight; 1 capsule per 20 lb./body weight daily thereafter—given in divided or single doses.

Continue therapy until patient is asymptomatic for at least 48 hours.

How supplied.—100 and 500.

Sulfamethoxypyridazine: MIDICEL ACETYL SUSPENSION (Pr), P. D. & Co.

Description.—Each 5 c.c. provides N¹-acetyl sulfamethoxypyridazine equivalent to 250 mg. of Midicel (sulfamethoxypyridazine). Butterscotch-flavour.

Indications.—For use in the treatment of bacterial infections.

Administration.—Children, 30 mg. per kg. of body weight (1 teaspoonful per 18 lb.) first day, followed by 15 mg. per kg. of body weight daily, but not to exceed adult dosage. Adults, 1 g. (4 teaspoonfuls) first day, followed by ½ g. daily. In severe infections dosage may be increased; see circular in the package.

How supplied.—4 fl. oz.

MISCELLANEOUS

UREVERT, Baxter

Description.—Lyophilized urea and travert.

Indications.—For reduction of intracranial pressure in conditions such as: brain tumours, acute glaucoma, cerebral oedema, central nervous system infections, head injuries.

NORMAL HUMAN PLASMA, M. S. D.

Description.—Normal human plasma, irradiated, 'Lyovac' is a satisfactory substitute for whole human blood in the treatment of certain conditions, in some of which it is superior. The plasma is restored to full volume by the addition of the specified quantity of sterile, pyrogen-free, 0.1% citric acid solution.

How supplied.—Packages to yield 50 c.c., 250 c.c., or 500 c.c. of restored plasma.

SURGICAL VENOPAK, Abbott

Description.—76-inch disposable venoclysis set with three injection sites. Packed in sets of 20.

REVIEW ARTICLE

DICOUMAROL DRUGS AND THE
PROBLEM OF HÆMORRHAGE*L. B. JAKES, M.A., Ph.D., F.R.S.C.,†
Saskatoon, Sask.

MODERN pharmacology aims to provide a scientific explanation of the clinical action of drugs. Anticoagulants first developed 25 years ago in Toronto have a well-established place in therapeutics. To understand the clinical problems presented by the use of these drugs requires an understanding of their pharmacology—clinical effects, distribution and metabolism, antidotes and toxicity. The present paper is a description of the pharmacology of dicoumarol and other indirect anticoagulants.

The classical indirect anticoagulant is dicoumarol, discovered by K. P. Link.¹ This and all the many compounds subsequently introduced into medicine are characterized not only by the fact that they have no significant effect on blood clotting when added outside the body, but also that the effect on blood coagulation is demonstrated by the change in the clotting time measured with added thromboplastin, the *prothrombin time*, developed by A. J. Quick. The tremendous developments in the study of blood coagulation in recent years have resulted in a great increase in the number of known factors involved in blood coagulation. While this has made untenable the view that the prothrombin time is a measure of the concentration of prothrombin itself, it has left unchallenged the view that increases in the prothrombin time are due to decreases in the concentration in plasma of proteins closely related to prothrombin and associated with it in its activity in coagulation. For simplicity, we can refer to this as the prothrombin complex and to these drugs as prothrombopenic drugs—drugs which cause an increase in the prothrombin time.

The effect on prothrombin time does not appear immediately after administration of these drugs. When a single dose of dicoumarol is given, it requires 24 hours for it to cause an increase in prothrombin time and the effect of a single dose of the drug on the prothrombin time will persist for five days. If we are to consider we understand the action of this drug, we must be able to explain the prolonged lag in the appearance of the effect of the drug on the blood, the increased prothrombin time, and the persistence of the effect, including the slow return of the prothrombin time to normal levels. It has been widely held that the lag represents the time required for the circulating prothrombin complex to be used up, and the time to return to normal as the time required for its

replacement. A great number of prothrombopenic drugs are available today. Many of these, such as Tromexan (ethyl biscoumacetate), warfarin and Marcumar (phenyl-hydroxycoumarin) are related to dicoumarol, being also substituted hydroxycoumarins. On the other hand, phenylindanedione (introduced on the North American continent after work in our laboratory)² is not a coumarin; it and a series of related compounds such as Dipaxin (diphenylacetylindanedione) are also active. When these compounds are given to animals or patients there are significant differences in the response obtained. When dicoumarol and phenylindanedione are given in single doses approximately the same increase in prothrombin time can be obtained, but the prolongation of prothrombin time is much greater with dicoumarol. Many chemical compounds closely related to dicoumarol or phenylindanedione, however, have no effect on the prothrombin time.

Site of Action of Prothrombopenic Drugs

Jakes and Spinks³ studied the site of action, using dicoumarol with a radioactive label. Radioactivity was found in blood, urine and gastrointestinal tract, but none was found in skin, muscle or viscera, except the liver. As much as 20% of the dose was found in the liver and by isolation it was demonstrated that the radioactivity was due to unchanged dicoumarol. Jakes and his colleagues⁴ compared in a number of species the effect of dicoumarol on the prothrombin time with the length of time dicoumarol remained in the liver. As shown in Fig. 1, the species in which a single dose of dicoumarol causes only a transitory change in prothrombin time show only a minimal amount of dicoumarol present in the liver for only a short time, while larger amounts of dicoumarol are found in the liver for much longer periods

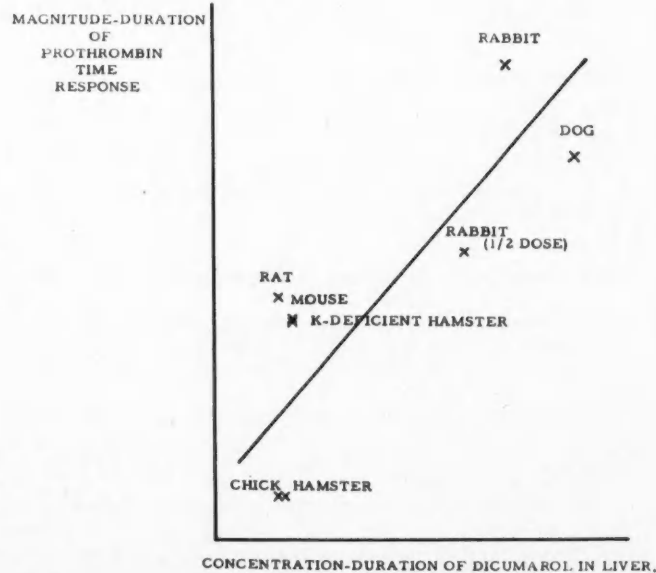


Fig. 1.—Relation between prothrombin time response and presence of dicoumarol in the liver. Relative areas of the response curves are plotted (as log values). Dicoumarol—5 mg./kg. Drawn from data in (4).

*A summary of lectures delivered before the Faculty of the Medical School, University of Birmingham, September 22, 1958; Department of Investigative Medicine, McGill University, March 2, 1959; and the Medical Faculty, University of Saskatchewan, April 22, 1959.
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in those species where there is marked effect on prothrombin time. Individuals in a given species also show marked differences in the prothrombin time response to a given dose of dicoumarol. Thus in rabbits, some show no change in prothrombin time with doses of dicoumarol which cause a pronounced increase in most animals, and hence rabbits can be divided into two groups, non-reactors with no change in prothrombin time, and reactors. When they were given C^{14} -dicoumarol, the drug in the nonreactor rabbits rapidly disappeared from plasma, blood, liver and muscle in a die-away curve. In reactor rabbits, the dicoumarol persisted longer in blood and tissues. In those animals which showed an increase in prothrombin time, the dicoumarol remained in the liver for three or four days. This difference in the liver was presumably responsible for the difference in concentrations of dicoumarol in the blood. Dicoumarol appears to be metabolized by the liver eventually, and therefore in those animals where there is a hold-up in the liver, its disappearance from the blood and body generally is slower. Van Cauwenberge and Jaques⁵ recently made the interesting observation that when such non-reactor rabbits are treated with ACTH, they will show increased prothrombin times with dicoumarol.

Millar *et al.*⁶ have studied blood and tissue levels of phenylindanedione (Danilone, Dindivan) in animals. Phenylindanedione disappears from the blood at a surprisingly rapid rate. Like dicoumarol, it can be recovered from the liver, and after intravenous injection much larger amounts of phenylindanedione than dicoumarol appeared in the liver immediately after administration. Up to 18 hours the amount remaining in the liver was about the same as for dicoumarol. On oral administration, absorption from the gastro-intestinal tract was relatively slow, although this may be complicated since intravenous injection showed some excretion of the drug in the bile with possible recycling. However, a very marked difference appeared between blood levels obtained after oral and intravenous administration of the drug. After oral administration, the concentration of phenylindanedione in the plasma was almost negligible, indicating rapid uptake by the liver. As with dicoumarol, the amount of drug fixed in the liver appears to be related to the effect observed on the prothrombin time, but we have not been able to obtain an exact correlation between liver levels and degree of hypoprothrombinæmia. It seems that a certain level or threshold of the drug must be reached in the liver. The fluctuations of the prothrombin time values in the blood do not appear to reflect fluctuations of the amount of the drug in the liver, although our methods of measurement of the latter are much less exact.

Many workers (originally Link) have attempted to identify the active groups in dicoumarol by testing various related compounds. Like Weiner⁷ we found that it is not sufficient to study the effect

of a single dose of the compound. For example, we found phenylindanedione quite disappointing in our early trials. It was only when we studied repeated doses every eight hours that we got a satisfactory response in dogs and rabbits. Hence a substance can be declared inactive only if no effect on the prothrombin time is detected when adequate blood levels have been demonstrated. Weiner⁷ and Pulver⁸ have done this for the metabolites of ethyl biscoumacetate (Tromexan) and found both compounds inactive, so evidently as slight a change as introducing a hydroxyl group in the ring, or a carboxyl on the methylene bridge, will render dicoumarol compounds inactive. On the other hand, when compounds as far removed as the indanediones are active, it is evident that considerable variability in chemical structure can still be accompanied by prothrombopenic activity. Link advanced the view that these compounds were degraded to the active compound. Salicylic acid, which he considered to be the active compound, is a weak prothrombopenic agent. It probably can affect prothrombin levels slightly through several actions, one of which is undoubtedly the conversion of small amounts to dicoumarol or a similar compound by bacteria of the gastro-intestinal tract, since Jaques and Lepp⁹ showed that in rabbits large doses of sodium salicylate intravenously had no effect on prothrombin time, but did increase it when given orally, and that succinylsulfathiazole abolished the effect.

Dicoumarol presumably inhibits an enzyme system in the liver. Martius¹⁰ has claimed that it inhibits oxidative phosphorylation. Lowenthal¹¹ in our department has confirmed this but observed that the effect is not shown by all prothrombopenic agents. He found that this action was reversed by cytochrome C but not by K_3 , that there was no difference with respect to oxidative phosphorylation, succinic acid oxidase, or cytochrome C oxidase in mitochondria and livers of animals treated with dicoumarol and those not treated, and that dicoumarol did not affect the increase in amount of tryptophan peroxidase produced by sodium salicylate, so that dicoumarol does not affect synthesis of new protein. Probably the effect of dicoumarol on oxidation mechanisms explains the toxic effects of dicoumarol on heart and blood vessels but not its specific effect on prothrombin.

Dicoumarol Drugs and Thrombosis

Dicoumarol drugs are not used simply to increase the prothrombin time of patients but to prevent thrombosis. Our original experiments in Toronto by Murray *et al.*¹² and Dale and Jaques¹³ successfully demonstrated that large doses of heparin and dicoumarol could prevent the formation of a thrombus in experimental animals, but evidence that reduction in the incidence of thrombosis depended on the degree to which the prothrombin time was increased has been lacking up to now. To establish a correlation between dose of drug

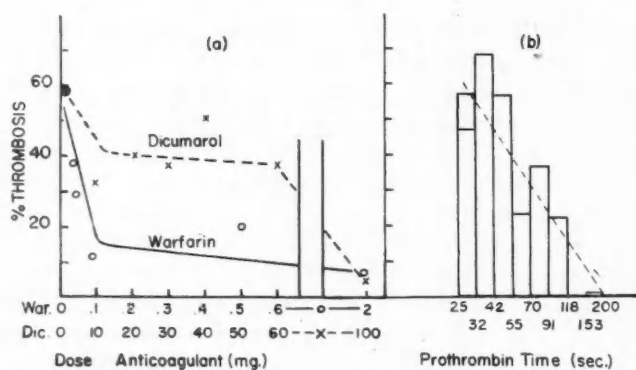


Fig. 2.—Relation between dose or prothrombin time following indirect anticoagulants and incidence of thrombosis. Thrombosis produced in jugular vein of rats. Reproduced by permission from *J. Clin. Path.* (14).

(or effect on coagulation) and the effectiveness of the agent in reducing the incidence of thrombosis, it is necessary to use large numbers of subjects with a reproducible incidence of thrombosis. Blake, Ashwin and Jaques¹⁴ have recently worked out a procedure in rats. By simple exposure of the jugular vein and the application of a little 4% formaldehyde to the outside of the vein, closing up the incision and examining it 24 hours later, 70% of the animals consistently developed a thrombus in this vein, readily demonstrated by visual inspection. It is then possible to test the efficacy of an anticoagulant as an antithrombotic agent. As shown in Fig. 2, when dicoumarol and warfarin were tested, warfarin was a much more effective prothrombopenic agent than dicoumarol, but both agents showed a considerable variation with individual animals with regard to the dose increasing prothrombin time. When the incidence of thrombosis was compared with the dose in milligrams of these two agents (Fig. 2a), the highest dose of both drugs reduced the incidence of thrombosis but there was no particular relationship between the degree of reduction and the dosage of drug. When the same animals were grouped on the basis of the change in prothrombin time produced in the individual rat by these drugs (Fig. 2b), a linear relation was obtained between the percentage reduction in thrombosis and the increase in prothrombin time. Therefore an actual linear relationship has at least been demonstrated in the experimental animal between reduction in incidence of thrombosis and increase in prothrombin time with prothrombopenic drugs.

Prothrombopenic Drugs and Vitamin K

The specific antidote for these prothrombopenic agents is vitamin K₁. Vitamin K₃ (menadione) is 2-methyl-1,4-naphthoquinone, while vitamin K₁ is the same with the long phytyl side chain in the 3-position. They have been called the synthetic and natural vitamins, but this differentiation is pointless, as today both compounds are obtained synthetically. When the effectiveness of the two compounds is compared with their ability to reverse the effect of dicoumarol on the prothrombin time

in the same patient, menadione has no effect, while administration of vitamin K₁ can result in a prothrombin time close to normal in less than 24 hours. Lowenthal¹¹ has recently examined this problem from the standpoint of how long it takes K₁ to act. When commercial K₁ preparations are given to rabbits with prothrombin times raised to 100 seconds (normal 15-17 seconds) by warfarin, the prothrombin time returns to a value of 20 seconds in two to eight hours. When K₁ is rendered suitably soluble by using Tween, the prothrombin time is reduced in 40 minutes and a shortening of the prothrombin time can be detected four minutes after the injection. Surely, if the generally accepted view is correct that the time for prothrombin values to return to normal levels after administration of prothrombopenic drugs is due to the synthesis of proteins of the prothrombin complex, then extensive replacement of these proteins in the circulation in 40 minutes means that we must revise our ideas of plasma protein synthesis.

The finding that only vitamin K₁ is therapeutically effective in restoring the prolonged prothrombin time after prothrombopenic drugs, while both K₃ and K₁ are equally effective as dietary supplements in the vitamin-deficient chick, suggests that either these are two fundamentally different actions or that K₃ is converted to K₁ before acting. Jaques and Dunlop¹⁵ showed that when menadione (K₃) is given to dogs simultaneously with dicoumarol it interferes with the rise in prothrombin time. Jaques and Spinks³ showed that K₃ causes a more rapid disappearance of C¹⁴-dicoumarol from the liver of rats, so that although K₃ is not an antidote for dicoumarol, it is an effective antagonist. Dogs with a bile fistula are usually assumed to represent cases of a simple K-vitamin deficiency. After some months the blood of such animals appears to be highly deficient in the prothrombin complex, including proconvertin. Fisher, Millar and Jaques¹⁶ showed that when the vitamins in equimolar doses are given orally the prothrombin time returns to normal, and in fact after K₃ administration it persists at normal levels for three weeks. When the blood is examined in the first hours after intravenous administration, using the proconvertin test as a sensitive index of changes in the prothrombin complex, the test values become normal in four to ten hours with both K₁ and K₃ and even more rapidly with Synkavite (the phosphate derivative of K₃). Hence the uniqueness of action of K₁ versus K₃ as an antidote for dicoumarol does not hold for other conditions of hypoprothrombinemia. We earlier concluded that the effect of prothrombopenic drugs is due to their fixation in the liver. While dicoumarol acts in the liver, it does not necessarily follow that the antidotal action of vitamin K₁ is at the same site. Jürgens¹⁷ observed in cats that after removal of the liver in dicoumarolized animals, K₁ rapidly reversed the prothrombin time. This suggests that K₁ can exert its effect outside

the liver. The rapidity of action of K_1 in the prothrombinopenia due to dicoumarol suggests an effect on cell permeability with release of the proteins of the prothrombin complex.

Side Effects and Toxicity of Dicoumarol Drugs

As these drugs accumulate in the liver, one would expect to see some evidence of disturbance of liver function, but the ordinary liver function tests all appear to give normal results. Irish and Jaques¹⁸ demonstrated that the plasma concentration of fibrinogen (the most sensitive test of hepatotoxicity) is affected by dicoumarol. In this respect, the latter is certainly a very mild liver toxin because an average dose will cause an increase in plasma fibrinogen, as for minimal doses of most hepatotoxins, and it takes abnormally large doses to cause the typical fall. Van Cauwenberge and Jaques¹⁹ observed in animals receiving dicoumarol, together with other drugs, an apparent reinforcement of drug action by dicoumarol. When using Dial (diallylbarbituric acid) in rats, good anaesthesia was obtained with no deaths in control animals receiving Dial alone, but rats on dicoumarol died before recovering from the anaesthesia. When rats received dicoumarol and reserpine, as judged by their general behaviour, the dose of reserpine had a much greater tranquillizing effect in the dicoumarolized rats than in the controls receiving reserpine alone. Finally, adrenalectomized animals maintained on saline all died of adrenal insufficiency in four days when given dicoumarol, suggesting an increased requirement for corticosteroids after dicoumarol. Jaques *et al.*⁴ found a specific uptake of dicoumarol by heart muscle. Kubo²⁰ and Lowenthal²¹ have found that dicoumarol is toxic to the isolated rabbit heart and this probably explains the symptoms of right heart failure observed by the early workers (cf. 13) in rabbits receiving extra large doses of dicoumarol.

Spontaneous Hæmorrhage

The major sign of toxicity with anticoagulants is spontaneous hæmorrhage. In our early experimental work with anticoagulants, we *never* saw animals develop hæmorrhage. In fact, it is amazing how completely some of these drugs can interfere with the blood coagulation system without any symptoms of hæmorrhage. Using phenylindanedione, we have maintained the prothrombin time at a level of 10 minutes (normal 10-12 seconds) for three and four months without any signs of hæmorrhage. A prothrombin time of 10 minutes must surely represent a complete blocking of coagulation and is much beyond values established clinically. The fact that hæmorrhage is a not too uncommon complication of clinical use of anticoagulants suggests that some important factor or factors in the production of hæmorrhage have been overlooked. Studies in our laboratory²¹ have demonstrated that stress constitutes such a hæmor-

rhagic factor. When rabbits receiving dicoumarol were exposed to the stress procedures of frostbite, insulin convulsions, or injection of 10% NaCl intraperitoneally, 50% died 60 to 72 hours later. On post-mortem examination, hæmorrhage could be demonstrated in most animals. We have termed this phenomenon death from spontaneous hæmorrhage, and have found that it can be produced by various combinations of treatment. The extensive hæmorrhage usually found post mortem might take the form of an extensive subcutaneous hæmorrhage. In some animals the pleural cavity was found to be filled with blood. Many animals showed marked pulmonary congestion and hæmorrhage, which on occasion appeared as patches of hæmorrhage over the lung. A few animals showed hæmaturia before death. Ecchymotic areas were frequently observed in the kidneys. Hæmorrhage has been observed in the peritoneum, in the intestine (sometimes due to a perforation), in the pericardium and in the uterus. One rabbit developed a hemiplegia of the left fore and hind quarters and there appeared to be a light hæmorrhage into the internal capsule upon examination of the fixed brain tissue. Bleeding from the nose and mouth was not common; when it did occur, the blood loss was certainly not sufficient to explain the marked paleness of organs found on post-mortem examination. In some animals, no frank hæmorrhage could be found. As the time and nature of death were the same and the extreme paleness of the organs indicated severe anæmia, we concluded that they also died from generalized blood loss.

The incidence of death from spontaneous hæmorrhage in rabbits when treated with anticoagulants together with stress procedures is remarkable. No animals died of hæmorrhage when given phenylindanedione alone. The degree of stress used was just below the M.L.D., so that about 10% of animals died immediately from the effects of stress. These did not show signs of hæmorrhage and there were no later deaths at the time when other animals died from hæmorrhage. In contrast to this, when rabbits received both indirect anticoagulants and stress 40-70% died 60-70 hours later. This was true with both phenylindanedione (Danilone) and dicoumarol and with all three types of stress.

The same phenomenon was observed in rats.¹⁹ When rats were given dicoumarol daily for five days, only 6% died, but when subjected to stressful procedures during this period, 50% of the rats died 24 hours later. As in the rabbits, little external hæmorrhage was observed but subcutaneous hæmorrhage was observed. The most common finding post mortem was hæmorrhage in the intestine and congestion and possible hæmorrhage in the lungs. Hæmorrhage was also observed in some animals in the peritoneum, kidney and adrenals and on the under surface of the brain. Other treatments than the 10% NaCl, used in doses known to deplete adrenal ascorbic acid and chol-

TABLE I.—RELATION OF PRODUCTION OF SPONTANEOUS HÆMORRHAGE TO HÆMOSTATIC MECHANISMS
(1) Blood coagulation (fibrin formation) (2) Clou hémostatique (platelet plugging)
(3) Vascular integrity and response (capillary resistance, vasoconstriction)

HÆMORRHAGE EXPERIMENTS		Hæmostatic mechanisms affected				
Treatment	Known effect of treatment	Dic.	Res.	Stress	Adr.	Hep.
Death from spontaneous hæmorrhage†						
Dicoumarol, Danilone.....	anticoagulant.....	1	+	+	+	-
Reserpine.....	removes platelet serotonin..	1;2	2	+	+	+
Frost bite, 10% NaCl i.p., Insulin convl..	decreases capillary resistance	1;3	2;3	3	-	-
Adrenalectomy, ACTH.....	decreases capillary resistance	1;3	2;3	3;3	3	+
Heparin.....	anticoagulant and antistress	1;1	1;2	1*;3	1;3	1
Hæmostatic mechanisms affected						

*But antistress. †30-100% mortality.

esterol, to increase steroid levels in blood and to decrease the circulating eosinophils, also caused the same type of hæmorrhagic death when combined with dicoumarol. About 50% mortality from spontaneous hæmorrhage was found on administering sodium salicylate, adrenaline and histamine with dicoumarol.

Trauma and adrenalectomy were introduced as factors in some experiments. Trauma increased mortality but did not change the conclusions. Thus, dicoumarolized rats showed 30% mortality on cardiac puncture, compared with a very low mortality with untreated rats, but the mortality was raised to 70% if the rats were also subjected to the stress of electroshock before cardiac puncture. When adrenalectomized rats maintained on 1% NaCl were given dicoumarol, they died within a week of adrenal insufficiency. If the rats received desoxycorticosterone, the signs of adrenal insufficiency did not develop but the rats still died within six days. In this case the rats died of hæmorrhage identical with that of intact dicoumarolized rats subjected to stress. Mortality was reduced slightly by whole adrenal cortical extract and prevented almost completely when these dicoumarolized adrenalectomized rats were maintained on cortisone or a somewhat larger dose of hydrocortisone.

It was possible to produce identical death from spontaneous hæmorrhage in animals without the use of anticoagulants and with no change in prothrombin time.²² When rabbits or rats subjected to the stress of 10% NaCl intraperitoneally were also given reserpine, 30% of the animals died of hæmorrhage 65-90 hours after the stress and reserpine, without any significant change in prothrombin time.

How do these treatments lead to hæmorrhage? In the dicoumarolized subject, is it due to the dicoumarol producing a greater effect on the prothrombin time? Prothrombin values were determined in all these experiments, and while sometimes an increase and sometimes a decrease occurred in the mean value, there was no relation between this and the mortality figure. The answer is actually one that has been known to workers on coagulation for many years—the multiplicity of factors in hæmorrhage and hæmostasis. Roskam²³ in particular has written on this but most authorities in the field have recognized it to a greater or lesser degree. Hæmostasis does not depend on any one single mechanism. There are at least three definite mechanisms (Table I)—the coagulation system, the platelets, the vascular component (vascular integrity and vascular response). Tocantins²⁴ has indicated that the relative importance of these three mechanisms is different at different levels of the vascular tree. Spontaneous hæmorrhage does not result if only one of these mechanisms of hæmostasis is blocked. For example, individuals with the rare condition of afibrinogenæmia may live for many years in spite of the fact that there is no possibility of the blood clotting. Patients on anticoagulants may shave without difficulty from hæmorrhage. These examples may be replicated many times. They emphasize that for such a serious physiological function as hæmostasis there is a very great physiological reserve. Hence, when animals bleed after treatment with dicoumarol and stress, it is due to the effect of the stress on a hæmostatic mechanism other than the coagulation system which has already been deranged by dicoumarol. Kramár²⁵ has demonstrated that stress

and adrenalectomy have a very marked effect on the ability of blood vessels to maintain their integrity as judged by the capillary resistance test. Haemorrhage results from combined treatment with dicoumarol and stress because after stress there is marked impairment of vascular integrity.

Our experiments on spontaneous haemorrhage are summarized in Table I. The various treatments to which experimental animals have been subjected are listed on the left-hand side and again across the top of the Table. In the upper right side is scored the occurrence of spontaneous haemorrhage. Along the diagonal corresponding to treatment with a single procedure, all values are negative (-); i.e., spontaneous haemorrhage does not occur or only to a slight degree (<10%). Away from the diagonal corresponds to treatment with a combination of procedures. Some of these show +; i.e., 30-100% mortality from spontaneous haemorrhage. Numbering the haemostatic mechanisms (1), (2) and (3) for blood coagulation, platelet plugging and vascular integrity, we can then indicate the haemostatic mechanisms blocked by the given procedure and this is entered in the lower left half of the Table. Dicoumarol as an anticoagulant blocks (1). Reserpine by removing serotonin from platelets presumably affects (2). Stress and adrenalectomy reduce the effectiveness of (3). No spontaneous haemorrhage results from these individual effects. When (1) and (2) are both disrupted by dicoumarol and reserpine together, haemorrhage occurs. When (1) and (3) are damaged by dicoumarol and stress together, or dicoumarol and adrenalectomy, spontaneous haemorrhage results. When (2) and (3) are damaged by reserpine and stress, haemorrhage occurs. On the other hand, stress and adrenalectomy act on a single mechanism or through a common pathway, and combining these does not result in haemorrhage. Finally, heparin acts as an anticoagulant but it does not cause spontaneous haemorrhage when the animals are subjected to stress. This presumably is related to the finding that heparin interferes with certain effects of stress.²⁶ It does produce spontaneous haemorrhage in adrenalectomized rats and in normal rats which have been treated with reserpine.

You may ask why we do not get 100% mortality from haemorrhage. In some experiments we do but there appears to be a large biological variation in response to the procedures used. For example, with dicoumarol we find reactor and non-reactor animals and the degree of mortality can be correlated with the severity of the hypoprothrombinaemia due to dicoumarol. When one gives a standard dose of a stress agent, it is quite evident that the strength of stimulus is different for different individuals and this is responsible for variation. There also appear to be different levels of interference with vascular integrity. There is also the possibility of one treatment interfering with the effect of the other treatment, since it is probable

that fibrin formation is involved in platelet clumping, platelet serotonin in vascular contraction, etc. However, we have found this rather coarse classification of mechanisms of haemostasis to stand up to experimental trial. As an operational principle, the manipulation of multiple factors to give an easily measured indicator—death from spontaneous haemorrhage—makes possible the assessment of the physiological factors governing haemostasis, including the hormonal and nervous components controlling the vascular factor, and the development of assay procedures to assess haemostatic agents. Equally important is the application of the principle in clinical medicine. More specifically, *spontaneous haemorrhage is not the natural accompaniment of anticoagulant therapy but rather a warning of the presence of some pathological process. Stress through its effect on blood vessels is one of the most common exciting causes of haemorrhage.*

This is a very quick survey of our recent contributions to this interesting field. The advances made could not possibly have been accomplished without the work of loyal colleagues and students. Owing to shortage of space it is not possible to mention them by name, but I would like to make special mention of Professor G. J. Millar, Dr. J. Lowenthal, our Professor of Chemistry, Dean J. W. T. Spinks, and Dr. H. van Cauwenberge, a visiting worker from Professor Roskam's department at Liège. His visit and most of this work were sponsored by the National Research Council of Canada. The work on thrombosis and the initial work on haemorrhage were supported by the Defence Research Board of Canada.

REFERENCES

1. LINK, K. P.: *Harvey Lect.* (1943-1944), 39: 162, 1944.
2. JAKES, L. B., GORDON, E. AND LEPP, E.: *Canad. M. A. J.*, 62: 465, 1950.
3. JAKES, L. B. AND SPINKS, J. W. T.: Factors affecting prothrombopenic action of dicoumarol and related drugs, *In*: Conference on blood clotting and allied problems; transactions of third conference, New York, 1950, Josiah Macy, Jr., Foundation, New York, 1950, p. 68.
4. JAKES, L. B. *et al.*: *Arch. internat. pharmacodyn.*, 111: 478, 1957.
5. VAN CAUWENBERGE, H. AND JAKES, L. B.: *Canad. M. A. J.*, 79: 536, 1958.
6. MILLAR, G. J. *et al.*: *Thromb. diath. hæm.*, 2: 236, 1958.
7. WEINER, M., BRODIE, B. B. AND BURNS, J. J.: Comparative study of hypoprothrombinemic agents; physiological disposition and chemical pharmacology of coumarin and indanedione compounds, *In*: Thrombosis and embolism; proceedings of the first international conference, Basle, 1954, edited by T. Koller and W. R. Merz, Benno Schwabe & Co., Basle, 1955, p. 181.
8. PULVER, R., MONTIGEL, C. AND EXER, B.: Über den Stoffwechsel von 4-Oxycoumarin-Derivaten, *In*: Thrombosis and embolism; proceedings of the first international conference, Basle, 1954, edited by T. Koller and W. R. Merz, Benno Schwabe & Co., Basle, 1955, p. 232.
9. JAKES, L. B. AND LEPP, E.: *Proc. Soc. Exper. Biol. & Med.*, 66: 178, 1947.
10. MARTIUS, C. AND NITZ-LITZOW, D.: *Biochem. Ztschr.*, 327: 1, 1955.
11. LOWENTHAL, J.: Unpublished.
12. MURRAY, D. W. G. *et al.*: *Canad. M. A. J.*, 35: 621, 1936.
13. DALE, D. U. AND JAKES, L. B.: *Ibid.*, 46: 546, 1942.
14. BLAKE, O. R., ASHWIN, J. G. AND JAKES, L. B.: *J. Clin. Path.*, 12: 118, 1959.
15. JAKES, L. B. AND DUNLOP, A. P.: *Canad. J. Res.*, E23: 167, 1945.
16. FISHER, L. M., MILLAR, G. J. AND JAKES, L. B.: *Canad. J. Biochem. & Physiol.*, 34: 1039, 1956.
17. JÜRGENS, R.: *Acta hæmat.*, 7: 143, 1952.
18. IRISH, U. D. AND JAKES, L. B.: *Am. J. Physiol.*, 143: 101, 1945.
19. VAN CAUWENBERGE, H. AND JAKES, L. B.: *Thromb. diath. hæm.*, 3: 45, 1959.
20. KUBO, H.: *Kumamoto M. J.*, 7: 73, 1954. Abstracted in: *Chem. Absts.*, 50: 8049e, 1956.

21. JAKES, L. B.: MOGENSEN, G. J. AND FISHER, L. M.: *Tr. Roy. Soc. Canada* (Ser. 3, Sect. 5), 50: 9, 1956.
22. JAKES, L. B. AND FISHER, L. M.: *Arch. internat. pharmacodyn.*, 1959, in press.
23. ROSKAM, J.: *L'hémotase spontanée*, Masson & Cie, Paris, 1951.
24. TOCANTINS, L. M.: *Ann. Surg.*, 125: 292, 1947.
25. KRÁMAR, J., MEYERS, V. W. AND WILHELMJ, C. M., JR.: *Proc. Soc. Exper. Biol. & Med.*, 89: 528, 1955.
26. HAMILTON, L. H. AND LOWENTHAL, J.: *Endocrinology*, 58: 546, 1956.

Association Notes

SUBSCRIPTIONS TO BRITISH MEDICAL JOURNAL

The British Medical Association informs us that the subscription rate to the *British Medical Journal* for members of the Canadian Medical Association has been raised from 2 guineas to 2½ guineas (£2.12.6d) as a result of revisions of subscriptions decided on by the representative body of the B.M.A. at the Edinburgh meeting. This low subscription rate, available to C.M.A. members, is the rate charged to B.M.A. members residing within the British Commonwealth.

MEDICAL SOCIETIES

THE AMERICAN ROENTGEN RAY SOCIETY

The 60th Annual Meeting of the American Roentgen Ray Society was held in Cincinnati, Ohio, September 22-25, at the Netherland Hilton Hotel. This meeting of the oldest scientific radiological organization in the United States attracted about 1500 radiologists from the U.S.A. and Canada.

The presidential address was given by Dr. Edward Neuhauser of Boston who succeeded Dr. B. R. Young of Philadelphia as president. Dr. Neuhauser made a sound plea for smaller meetings in medicine. He said that unless the numbers attending meetings were kept down and ample opportunity was given for discussion, the postgraduate education involved could not be effectively carried on. He added, "For years the major societies in medicine have been burgeoning in attendance; many take pride in the number of registrants. Unfortunately, more registrants don't necessarily mean a better meeting. . . . Smaller meetings usually held on an informal basis can have free discussion of completed studies or work in progress. Comment and criticism are invited. It is hoped that these scientific organizations will be kept small by firm and hard-minded admission committees."

A scientific highlight of the meeting was the annual Caldwell Lecture, honouring the memory of the late Dr. Eugene W. Caldwell of New York City, a pioneer in medical radiology. This year's lecturer was Dr. Donald L. McRae, associate professor of radiology, McGill University, who spoke on the significance of abnormalities of the cervical spine. Another striking feature of the meeting was the presentation of a very comprehensive motion picture on the medical use of

radiation. This picture, "Radiation; Physician and Patient", had been shown at the scientific assembly of the American Medical Association in June. The film is available for showing from the American Medical Association Film Library, the United States Public Health Service or the American College of Radiology, Chicago.

LETTERS TO THE EDITOR

DR. W. E. GALLIE

To the Editor:

It is well known to many of your readers that Dr. Gallie initiated the first formal training program for surgeons in Canada. Not so well known however is the fact that over the past 25 years the graduates of this training program have gathered once a year for a meeting with Dr. Gallie at which original work done by the former residents was presented to the group. For many of those participating this afforded them an opportunity to present their work; for all it was an opportunity to renew old friendships; however, for most of us who lived at a considerable distance from Toronto, it meant something far more than this. It was a sort of pilgrimage to be with our former Chief for two days.

Repeatedly I have thought about the profound influence exerted by this great man, not only on trainees in surgery, but also on students in medicine and surgeons in general throughout Canada and the world. I have tried to analyze what he meant to me particularly. Now that he has gone, it is prudent and timely to reflect on the great influence which he had on my own career. I would say that it was not that he was such a great surgeon, not that he was such a profound investigator and contributed many procedures of great importance to surgery in this world, nor that he was such a great teacher. What then are the influences that he had upon me in particular? He had attracted good teachers under his professorship who taught us much of our knowledge of surgical technique, diagnosis, and surgical patient care, but I think his greatest influence was "the man himself". His honesty, integrity and humility were qualities which one did not learn from his lectures or writings. These were qualities which we all strove to emulate but which few of us have been able to develop to anywhere near the degree possessed by him. One could not be in his presence without feeling his influence in these respects, and even to feel them once a year at our annual meeting served as a great stimulus for the ensuing 12 months until we would gather again. He was forthright in his opinions, but he was also kindly. He was a friend to anyone who had even slight contact with him. On the one hand he was regarded as "God himself" and on the other hand, "father confessor and a true friend". He was never too busy to talk to one of his trainees and his words were always compassionate and never berating. His tireless energy and great kindness towards his patients were something that you could not help but absorb as you made rounds with him.

He taught all of us to be good teachers and good surgeons but by simple example he also taught us the finest qualities of man. I am sure these will be enduring even though he has passed on. I am sure they will

pervade the atmosphere of our meeting room annually in the future. He will be there even though we cannot see him.

HROLFE R. ZIEGLER, M.D.

797 Elmwood Avenue,
Rochester 20, N.Y.,
October 15, 1959.

HEALTH EDUCATION

To the Editor:

I was disturbed by your editorial "Educating the Public" in the September 1 issue of the Journal. I thought it was good because I believe that it pretty accurately reflects the views of that great mass of more or less educated people who earn their living by treating the sick.

This editorial marches in several directions so that one finds it difficult to be sure just what it is really discussing. This is why I like it. It reveals the confused equivocal attitude of the medical profession about "health education", "disease education", "positive health" and education about illness—to say nothing about a "socially acceptable equivalent of a mediæval execution".

You see, this editorial hits me where I live. After a quarter of a century in other branches of medicine I have for the past dozen years or so been specializing in public health. Public health is no longer a police action to control infection. Today, public health is predominantly health education. Am I therefore to regard myself and the organization I direct as not deserving outright condemnation but as doing something that has strong overtones of mythology, bogus talk about "positive health", charlatanism and simple "showmanship"?

During the war I had with me a young Canadian gynaecologist. He had had his specialist training in the United Kingdom. I asked him what he thought of public health. "Oh," he said, "those guys don't do anything—that's just a racket." And again quite recently a leading Manitoba surgeon encountering a young colleague said: "Well, what are you doing now?" And on being informed by the colleague that he was in public health, said: "Well, what is public health doing?" When the young doctor hesitated our senior colleague remarked: "Well, whatever it is, I guess it's not very important!" I mention these incidents because the whole flavour of your editorial suggests that they are not atypical.

One submits that today there is a solid body of information plus an impressive mass of suggestive evidence that a considerable degree of well-being by a considerable percentage of our people can be achieved if this is desired. I know doctors are under pressure to practise "humbug"; I know charlatans are abroad and that a good many people "enjoy" poor health. But does this not underline the need to educate the uninformed and the misinformed?

Surely we do not want to see our country regarded as a sort of "animal farm" populated by a mindless mass of livestock treated by expert impersonal veterinarians operating in state-supported abattoirs into which every fifth person, and sometimes every other

person, can be herded annually. This is a spectacle I have seen unfolding before my very eyes these past 10 years. It is not a pretty picture but I know of no way to change it save by health education.

In conclusion, may I say that in the light of your editorial perhaps it is time for the medical practitioner to take a long second look at (a) his attitude towards the patient and (b) his attitude towards those who, however ineptly, are trying to promote positive health and to instruct regarding the real nature of disease.

G. KINNEARD, M.D.,

Director, Regional Health Services Branch,
Department of Public Health,
Health and Welfare Building,
Regina, Saskatchewan,
October 14, 1959.

PARAPLEGIC EMPIRE GAMES

To the Editor:

It is the intention of the Paraplegic Association of Western Australia, acting through Royal Perth Hospital, Perth, Western Australia, to arrange for and conduct a Paraplegic Empire Games just prior to the Empire Games to be held in Perth in 1962.

I would be most grateful if you could make mention of this fact in your Journal, inviting any person interested to communicate with me over the matter, for it is hoped that teams will reach Perth from all over the Commonwealth countries.

Further details will be supplied on application, as to who is arranging for the team in each particular country.

I would be most grateful for your assistance in this matter as my Committee hope that this will be made as widely known as possible.

G. M. BEDBROOK,
Paraplegic Association of
Western Australia,
Paraplegic Unit, Shenton Park Annexe,
Shenton Park, Western Australia,
September 7, 1959.

PUBLIC HEALTH

RESEARCH AND STATISTICS

The Annual Report for 1958-59 of the Research and Statistics Division of the Department of National Health and Welfare shows that major emphasis during this year was on research connected with the development of hospital insurance. Out of this, two publications on voluntary medical insurance and voluntary hospital insurance in Canada were prepared and a study on hospital care and transition, designed to summarize the principal characteristics of Canadian hospital services, including their financing at the commencement of the federal-provincial hospital insurance program, was largely completed.

Other studies concerned the variability of radioactive strontium estimates in dried milk samples, a study of the health of uranium miners, a long-term study of mortality in D.V.A. pensioners in relation to smoking habits and occupational and residential history, a follow-up study of pelvimetry examinations at an Ottawa hospital to determine

possible relationships to leukaemia in the offspring, a national survey of psychiatric services in general hospitals, and research on chronic illness, dental health and civil defence.

Other publications were concerned with the administration of public health in Canada, rehabilitation of the disabled, economic security for the aged and other aspects of welfare.

SURVEILLANCE REPORTS OF EPIDEMIC
OR UNUSUAL COMMUNICABLE
DISEASES

PARALYTIC POLIOMYELITIS
CANADA

During the week ending October 3, 1959, 112 cases of paralytic poliomyelitis were reported to the Epidemiology Division, representing again a slight increase over the 109 cases reported in the preceding week. The expected down-

ward trend following the 139 cases reported in week 36 has not yet fully materialized. The high number of cases reported in the week ending October 3 was due mainly to a sudden upswing in the number of cases reported in British Columbia from 4 cases in week 38 to 19 cases in week 39.

Although the number of cases admitted in Montreal hospitals are definitely on the decrease, the incidence in the rest of the province of Quebec still remains at a high level.

Ontario has shown a decrease to 13 in the number of cases reported this week from the high of 19 the previous week.

MEASLES
EASTERN REGION

Eighty-seven cases of measles have occurred at St. Augustine, Saguenay County, Quebec, in an Indian reserve with a population of 93. Ten are seriously ill with pneumonia and one woman aged 79 died. An old man and a baby were evacuated to hospital. It is expected that the remaining unaffected six Indians will probably develop measles in the near future.

PARALYTIC POLIOMYELITIS IN CANADA*
40TH WEEK—ENDING OCTOBER 10, 1959

	Reported cases					Deaths	
	1959			1958		1959	1958
	This week	Last week	To this date	This week	To this date	To this date	To this date
Canada.....	88	112	1,294	13	186	117	19
Newfoundland.....	(a)	5	112		4	8	Nil
Prince Edward Island.....		2	4				
Nova Scotia.....			2				
New Brunswick.....	3	6	40		1	5	1
Quebec.....	62	58	843	6	53	69	1
Ontario.....	6	13	153	4	16	14	6
Manitoba.....	1	2	22	3	84	2	8
Saskatchewan.....	8	3	28		1	2	
Alberta.....	5	4	33		19	3	1
British Columbia.....	3	19	46		8	9	2
Yukon.....			1			1	
Northwest Territories.....			10			4	

*Weekly returns based on telegraphic reports by provinces.
(a) Figures not available.

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BRITISH COLUMBIA

From Quesnel, it is reported that three cases of paralytic poliomyelitis have occurred in the same family, all in children under 13 years of age; one died.

INDIAN AND NORTHERN HEALTH SERVICES

Between September 5 and 19, 1959, six cases of paralytic poliomyelitis were reported in Northern Manitoba, five among Indian children, the youngest being 6 months and

ORNITHOSIS
BRITISH COLUMBIA

A clinical diagnosis of ornithosis was made in a 30-year-old man from Comox. The family lives in a trailer with two budgerigars recently purchased in Vancouver. One of the budgerigars died and the other is sick.

EPIDEMIC PLEURODYNIA
BRITISH COLUMBIA

Ten cases of epidemic pleurodynia (Bornholm disease) have occurred in the last two weeks at Lake Cowichan, affecting 8 young children, one 16-year-old girl and one adult. Virus studies will be attempted.

TETANUS

Four reports of tetanus cases have been received. One patient was a girl aged 8 years, from Bartlett's Harbour, St. Barbe District, Newfoundland; another was a woman aged 56 years, from De Salaberry, Manitoba. A 9-year-old boy from Cardston contracted tetanus after stepping on a nail in a barnyard. Onset on June 17, 1959; died June 19, 1959. He had received D.P.T. toxoid and had a booster in February 1959. The fourth case was in an Indian woman, aged 37 years, from Ashcroft, B.C.

WHOOPIING COUGH
MANITOBA

At the Nelson House Indian Reserve, 24 cases of whooping cough have been reported, all in children born between 1953 and 1959. One child died at Norway House Hospital.

BACILLARY DYSENTERY
ALBERTA

A surveillance report concerning an outbreak of bacillary dysentery in the Picture Butte area states that 68 cases occurred during September. From 13 stool specimens, *Shigella sonnei* was isolated.

TRICHINOSIS
SASKATCHEWAN

One adult male.

Epidemiology Division, Department of
National Health and Welfare, Ottawa.

October 10, 1959.

OBITUARIES

DR. JONATHAN C. MEAKINS
AN APPRECIATION

R.C. writes:

Canadian medicine has suffered a great loss in the death of Dr. Jonathan C. Meakins, a man of indefatigable energy to whom work was a pleasure to be enjoyed with zest and vigour and who set himself a program of work which would have been beyond most men's will and ability.

It was during the First World War that he became known as a sound physician who was also a brilliant investigator and who had the drive, energy and personality of the born leader. It did not surprise his friends when soon after his return to Montreal he was offered the Christison Chair of Therapeutics and Clinical Medicine at Edinburgh University.

In Edinburgh he was one of the first to introduce scientific methods of research into the Royal Infirmary, and the laboratories which he planned remain a tribute to his energy and foresight. He also struck a new note in the professoriate. It would not be unusual for him and his charming wife to enjoy a jovial evening with the students, and next morning deliver a fascinating lecture on the application of physiological principles to disease or conduct a breezy ward round, attended in those congested post-war days by 30 or 40 clerks. His life in Edinburgh was a full one and yet he found the time to write the first book on respiratory function in disease and was a member of Barcroft's expedition to the Andes which made the first comprehensive study of the effects of high altitudes on man.

On his return to Montreal as Professor of Medicine at McGill University and Physician-in-Chief at the Royal Victoria Hospital he made many changes in the old order. Naturally he met with some opposition. This only served to strengthen his confidence in the merit of his plans and was treated as a challenge which he met with characteristic determination. He quickly established himself as one of the leaders of medicine on the North American continent.

Dr. Meakins will be remembered by his colleagues for his magnetic and forceful personality and the prominent part he took in Canadian and North American medicine.

He will be remembered also by the loyal band of those he trained, for his friendly leadership, his integrity and the stimulation of his quick and accurate mind.

But long after his friends and colleagues have followed him, he will be remembered as a pioneer in applying scientific methods to medicine. He will take his place in medical history as the first to make an organized effort to investigate the disturbances of function which occur in diseases of the lung, an effort which culminated in the publication in 1925 of his book, *Respiratory Function in Disease*.

His name will also be recorded in the annals of Edinburgh University and McGill University as the person who introduced an atmosphere of scientific inquiry and research into their teaching hospitals.

D.M.D. writes:

Those of us who knew Jonathan Meakins when he was in Edinburgh heard of his death with much sorrow. Sir Thomas Fraser was the last Professor of Materia Medica in Edinburgh to hold a clinical charge and when he died his Chair was split into one of academic pharmacology, to which Arthur Cushny succeeded, and into one of clinical therapeutics to which Meakins was appointed. I was a student when he arrived and well remember the excitement of his advent for, though he came to us after the First World War, Edinburgh and its medical school remained somewhat Edwardian: horse cabs had not yet disappeared from the streets, some physicians still came to hospital in top hats and morning coats, their clinical charges were largely independent hierarchies between which there was little intercommunication, and when they went out to dinner it was in a white tie and a stiff shirt. Into this atmosphere, which was metaphorically somewhat stiff-shirted also, burst this young, good-looking, vital and enthusiastic new professor, bringing a breath of the laboratory and the new world into clinical medicine. He was the first non-gold-headed cane physician to hold a Chair in Scotland and one of the first in Britain—questioning and not authoritarian, believing that medicine was a science as well as an art. Perhaps at times he found his senior Edinburgh colleagues a little alien and stuffy and was glad when the call came to him to return to McGill as Professor of Medicine; but during the few years he was with us he was immensely stimulating to the young and lit a lamp of clinical science which he would have been glad to see burning brightly today. He was not the sort of man to have tolerated old age and senility with equanimity for he always warmed both hands before the fire of life and when it sank I am sure he was ready to depart. All the trumpets will sound gaily for him on the other side.

DR. H. O. BOYD, 95, died at his home in Bobcaygeon, Ont., on August 9. Born in India, he spent part of his early life in England and came to Canada when he was 16. Dr. Boyd received his medical education at the Trinity College Medical School, Toronto, graduated in 1897, and started practice in Bobcaygeon shortly afterwards. For three years in the First World

War he was in charge of a military hospital in France and was decorated by the French Government for his services. He retired from active practice some years ago.

Dr. Boyd is survived by his two daughters.

DR. JAMES L. BURNS, 78, died on September 13 at the Toronto East General Hospital. He was born in Palmerston, Ont., and became a school teacher for a short time before studying medicine. Dr. Burns attended the University of Toronto, where he graduated in medicine in 1907. After interning at Owen Sound, he practised at Simcoe before opening his practice in Toronto in 1910. In 1929 he joined the staff of the Toronto East General Hospital as head of the Department of Obstetrics and Gynaecology, a post which he held until his retirement in 1948.

Dr. Burns is survived by his son, Dr. John L. Burns of Toronto.

DR. CHARLES COWEN GURD, 86, died at Matane Hospital, P.Q., on August 22. He had been on vacation at nearby Metis Beach. A native of Montreal, Dr. Gurd was a graduate of McGill University in 1897. During World War I he served overseas with the R.C.A.M.C. and on being invalided out joined the staff of the old Western Hospital, where he was attached to the Department of Obstetrics and Gynaecology. When the Western Hospital was amalgamated with the Montreal General Hospital, Dr. Gurd was transferred to the staff of the latter hospital. On his retirement, he was appointed to the consulting staff of the Montreal General.

Dr. Gurd is survived by his widow and two sons.

DR. L. R. HILL, 64, a former medical officer of the Toronto Fire Department, died after a heart attack on August 21 at Sault Ste. Marie, Ont. Born in Toronto, he received his medical education at the University of Toronto, where he graduated in 1916. In the First World War he served overseas and was wounded in German East Africa. During World War II Dr. Hill was in Iceland and Britain as medical officer with the Royal Regiment of Canada, and was later posted to Newfoundland as Senior M.O. with the rank of lieutenant-colonel. Between the wars, in addition to his post as medical officer to the Toronto Fire Department, which he held from 1925 to 1947, Dr. Hill had a large general practice. For the past 11 years he lived in Bruce Mines, Ont., where he was the only physician.

Dr. Hill is survived by his widow and two sons.

DR. J. GAETAN KIRKLAND, 57, died at the Laval-sur-le-Lac Golf Club, P.Q., on August 27. A medical graduate of the University of Montreal in 1930, he was medical adviser to the Canadian Pacific Railway and also to the Metropolitan Life Insurance Company.

He is survived by his widow.

DR. BERNARD C. SULLIVAN, 65, died at the Halifax Infirmary, N.S., on August 10 after a brief illness. A native of Toronto and a veteran of World War I, he completed his medical training at the University of Toronto and graduated in 1920. In 1940, Dr. Sullivan moved to Halifax, where he became medical officer in charge at Halifax harbour.

He is survived by his widow, two sons and a daughter.

PROVINCIAL NEWS

ALBERTA

The annual meeting of the Alberta Division of the C.M.A. was held on September 28, 29, 30, and October 1 in the Macdonald Hotel, Edmonton. Registration reached the high level of 400. Guest speakers were: Dr. E. Bruce Tovee, assistant professor of surgery, University of Toronto; Dr. B. L. Hession, internist, University of Western Ontario; Dr. E. M. Jellinek, secretary-general, International Institute for Research in Problems of Alcohol, Geneva, Switzerland; and Dr. W. S. Simpson, Topeka, Kansas. Dr. Simpson is a 1948 graduate of the University of Alberta who went to the Menninger Clinic for advanced work in psychiatry.

The retiring president, Dr. J. W. Macgregor, installed his successor, Dr. W. C. Campbell of Medicine Hat. Dr. E. F. Donald, Edmonton, is the president-elect.

At the dinner which is staged annually by the University of Alberta Medical Alumni Association with Dr. A. V. Follett, Calgary, as president, the class of '34 was fêted. Eight of the 24 who graduated in that year were present. At this dinner, Dr. John W. Scott was honoured on his retirement from the post of Dean of the Faculty of Medicine at the University of Alberta, a position which he had held for 26 years. To honour Dr. Scott, the John W. Scott Award has been set up by the Medical Alumni Association. This will be offered to "individuals who, by the time of graduation, have shown themselves to possess those characteristics of scholarship, leadership and character that not only make them outstanding among their fellow students, but also indicate that they should become leaders in the medical profession". Selection of the recipients will be made by a committee on which will be represented Faculty, students and alumni. The award will consist of a medal and a cash prize of \$250. Only one student will be selected in a single year.

At the business meetings, some of the committee reports produced vigorous discussion with particular regard to the changing pattern in medical economics. One resolution took great exception to the TV filmettes by which the C.M.A. Central Committee on Public Relations has been promoting the medical profession. As many of those present had not seen these filmettes, some were obtained from the CBC in Winnipeg and run at the meeting. A resolution was passed requesting that the C.M.A. re-examine the policy with respect to these TV releases on the grounds that they constitute advertising and place the medical profession in the same class as others who advertise their healing powers.

Calgary Diagnostic Centre.—Dr. J. Donovan Ross, Minister of Health in the Alberta Government, was present at the meetings and discussed the proposed Foothills Provincial General Hospital which the government is building in Calgary. The purpose of this is to supply Calgary with needed hospital beds as well as to offer to the people of the southern part of the province the services which the University of Alberta Hospital gives to those in the north; that is, a first-class centre in physical medicine, and a consultant centre to which the southern doctors can send the estimated 1-2% of their patients with whom they need help. This Centre will be in a building adjacent to the

700-bed hospital. The hospital will also offer an educational program for interns, nurses and attending staff. The heads of departments will be on a geographical full-time basis; the minister has denied that this constitutes state medicine since this is an educational institution. He said that the doctors of Calgary will have courtesy staff privileges while some will be part-time consultants so that the referral centre will be no more than a supplement to the good services that Calgary already has.

Work has not yet started on the new hospital but the Board has already been appointed, as have the three key administrators: the medical administrator, the business administrator and the superintendent of nurses. These officials can work with the architects to develop plans related to the function of the institution. The Centre will be built near the campus of the University of Alberta at Calgary at a cost of ten or more million dollars.

Company Sick Benefit Plans

A company planned to give its employees full medical benefits plus several ancillary services such as drugs and sick pay. It wished to have the doctors bill the company direct on a basis of 90% of the fee schedule. This Division is against the principle of tailoring contracts to the needs of the various companies, and medical services can be provided at 100% of the fee schedule or through M.S. (Alberta) I.

Hospital Relations

Some revisions in the Hospitals Act are felt to be of significance. (1) "The Lieutenant Governor in Council may, *after consultation with* representatives of the Associated Hospitals of Alberta, the College of Physicians and Surgeons of Alberta, the Alberta Association of Registered Nurses, and the Alberta Pharmaceutical Association, or any of them as circumstances may require, make regulations." It is apparently the first time that the Government has gone on record and actually stated that it would consult with representatives of the medical profession. (2) The minister may requisition the hospital record of any hospital patient. If he uses the committees of the Alberta Division as consultants, this will greatly aid the work of the committees on maternal mortality, surgical and anaesthetic deaths, and perinatal mortality, since prior to this year there was no regulation to make these records available, and at times the co-operation of the physician concerned was far from complete.

Rehabilitation

The Minister of Health reported that as a result of the recommendation of last year's committee that rehabilitation centres be set up in Calgary and Edmonton, the government had approved the setting up of a fact-finding committee but not yet the founding of the pilot centre that the committee recommended.

Legislation, Constitution and By-laws

The functions of the Council of the College and those of the Board of Directors of the Alberta Division, C.M.A., are not definitely delineated in the constitution, and there is some overlap. Since the number of

physicians willing to serve is limited, it is felt that some change in the constitution is necessary, with three possibilities: (1) the setting up of two distinctly separate organizations, as is the case in British Columbia; (2) the amalgamation of the two organizations into one body as in Saskatchewan; (3) the continuation of two organizations on an interlocking basis with the responsibilities of the Division being restricted to education. The problem will be studied through the winter and discussed in the districts, so that a definite recommendation can be brought in next year.

New Business

In view of the fact that expired air resuscitation techniques have been shown to be much superior to other manual methods, yet the latter are still being advocated by first-aid organizations, a resolution was passed recommending that the C.M.A. make a report on the effectiveness of various methods of artificial respiration and communicate their findings to those organizations which have assumed lay instruction in this field.

College of Physicians and Surgeons

In his report to the College, the president, Dr. J. B. T. Wood of High Prairie, recommended that the possibility of constructing a building to house the offices of the Division and the College be investigated.

W. B. PARSONS

ONTARIO

Dr. E. M. Jellinek, who is on the staff of the University of Toronto and the Alcoholism Research Foundation of Ontario, received the first Gold Key Award presented by the National Council on Alcoholism of the United States for outstanding service in alcoholism prevention and treatment. His award was presented at a dinner in the Waldorf-Astoria Hotel, New York.

Dr. Gustave Gingras, professor of physical medicine and director of the School of Rehabilitation, University of Montreal, addressing the annual meeting of the Rehabilitation Foundation for Poliomyelitis and Orthopaedically Disabled in Toronto, said that three out of every 100 of Canada's population between 14 and 64 years old are so disabled that they cannot qualify for competitive employment. During the last year the Foundation spent \$470,519 helping 1200 persons in Ontario.

Dr. John Bowie, bacteriologist at the Royal Infirmary, Edinburgh, has recently been visiting laboratories in Montreal and Toronto and will go on to Ann Arbor, Erie and Cleveland where he will observe methods of hospital sterilization and confer with manufacturers of autoclaves. His special interest is hospital cross-infections and methods of sterilization. He spent several war years in Iran and Iraq and in 1943 was active in the laboratory investigation of the Teheran typhus epidemic among Persian coolies when two Indian Army hospitals handled 2600 cases of classical typhus during a ten-week epidemic.

LILLIAN A. CHASE

The Annual Dinner of the Toronto Academy of Medicine was held at the Royal York Hotel on October 6. After the invocation had been pronounced by Rabbi

A. Feinberg, the new president Dr. Harold Pritzker was installed, and the past-president Dr. R. C. Laird was presented with a past-president's pin by Dr. T. C. Routley. Dr. Adrian Anglin, vice-president, then presented the two golf trophies: the F. N. G. Starr cup to Dr. W. J. B. Maxwell and the W. E. Gallie trophy to Dr. E. J. Trow. The title of the president's inaugural address was "Challenges of Today". After reviewing some of the less agreeable aspects of modern society, Dr. Pritzker said that signs were not wanting of a return to the old virtues of sound education, thrift and so on. He felt that doctors should be prepared to speak out boldly, as they had done in the early days of the Academy, on matters of medical importance to the whole community. This meant of course that they must play their part in medical organizations, such as the Academy of Medicine. The chief problem before the Academy at the moment was one of housing; both the very fine collection of objects in the museum and the equally valuable library were desperately short of space, and the problem of providing additional housing was urgent.

QUEBEC

Early in October the Board of Administration of the Montreal Children's Hospital held its Annual Meeting. Mr. S. M. Finlayson, president, announced that the deficit from hospital operations in the year ending last May amounted to \$325,000 as compared with \$494,000 in the previous year. This is an almost 30% improvement which he described to be due to three major factors: first, the increasing occupancy and use of the hospital facilities; second, modification of hospital charges to meet increasing costs; and third, improvement in routine efficiency. He also reported that the cost per patient day rose to \$24.18 from \$22.95 the previous year. This again is a demonstration of the precarious financial status of some of the hospitals in this province.

It has been announced that the Parc Savard Hospital in Quebec City, which has been maintained as a quarantine and immigration hospital by the federal department of National Health and Welfare, has been transferred to the Province of Quebec. The Hon. J. W. Monteith announced that the immigration requirements will be handled in future at the new Federal Medical Centre at Wolfe's Cove, Quebec, while required quarantine facilities will be provided in co-operation with provincial health authorities. This brings to a close the long history of Parc Savard with its association with Canadian immigrants. This reporter has been advised that the hospital will continue to be operated as such, apparently through the provincial department of health.

A further \$990,600 in federal health grants has been awarded to Quebec hospitals. Of this, \$395,000 will go to construction of a new hospital in the Montreal area, the LaSalle General Hospital. This will be a one-storey building composed of six wings, and will accommodate 136 active treatment beds, 35 bassinets and six interns' beds. The hospital is scheduled for completion in 1960 and will serve residents in Ville LaSalle, Ville St-Pierre, Caughnawaga, Châteauguay, Ville-Emard and Côte St-Paul. About \$117,000 of the fund has been allocated to

the Montreal General Hospital towards the cost of two more floors on the wing for medical and surgical laboratories. Construction of this is now almost complete.

About \$327,000 of the fund is assigned to the construction of a new hospital for chronically ill male patients. This will be built at St-Louis-de-Courville near Quebec City. The remaining funds are awarded as equipment grants to a number of existing hospitals in the province.

On October 2, Dr. Michael Rand of the department of pharmacology, University of Oxford, delivered a special lecture in the Medical Building of McGill University under the sponsorship of the department of pharmacology of McGill University and of the Montreal Physiological Society. His subject was "New concepts of the mode of action of sympathomimetic amines and of sympathetic transmission." Dr. Rand is an Australian who has just completed two years of work at the University of Oxford in Professor Burn's department. At the present time he is at the University of Vermont.

Dr. Rand presented an excellent review on the mode of action of sympathomimetic amines with particular emphasis on the work that has been carried out over a number of years by Professor Burn and his associates at the University of Oxford. The implication which he emphasized, and is largely based on the work that he has carried out in association with Professor Burn, would seem to suggest that all post-ganglionic sympathetic nerves carry some cholinergic fibres. The primary function of these latter is to supply the acetylcholine which in turn acts on the noradrenaline stores to release this latter to act on muscles. The obvious implication from this is that all post-ganglionic sympathetic nerves are really cholinergic. It should therefore be quite obvious that a very lively discussion followed the presentation of this exceedingly stimulating address. Professor K. I. Melville, head of the department of pharmacology at McGill, chaired the meeting.

On Monday, October 5, Professor Leslie J. Wits, Nuffield professor of clinical medicine at Oxford University, delivered the seventh annual Francis Shepherd Memorial Lecture at the Montreal General Hospital. He spoke on "Achlorhydria and anaemia". Professor Wits began with the early history of development of our knowledge of gastric function. This has a rather close association with Montreal, through the French Canadian voyageur Alexis St. Martin, the subject on whom Dr. William Beaumont, a U.S. Army Medical Officer, conducted studies of the digestive processes for a period extending for some 11 years in the mid-nineteenth century. Reviewing methods and procedures that have been developed, Professor Wits said that investigation of the secretory capacity of the stomach was greatly advanced by the augmented histamine test and by the estimation of intrinsic factor from the absorption of tracer doses of radioactive vitamin B₁₂ given by mouth. In addition, the morbid anatomy of the stomach can now be studied by gastric biopsy. The so-called tubeless methods of gastric analysis, in which azuresin (Diagnex) is given by mouth or uropepsinogen is estimated in the urine, enable us to screen populations and pick out cases for more elaborate study. Use of these methods has shown

that achlorhydria is uncommon and is practically always associated with gross changes in the mucosa of the stomach. A substantial fraction of subjects with complete achlorhydria can be regarded as suffering from latent or preclinical pernicious anaemia.

It is now technically as easy (or easier) to demonstrate loss of intrinsic factor as to demonstrate complete achlorhydria. There are several pieces of evidence that loss of intrinsic factor may sometimes precede achlorhydria in the development of pernicious anaemia. Indeed, in juvenile pernicious anaemia free HCl is usually present whereas in adult pernicious anaemia free HCl is probably always absent. Measurement of intrinsic factor is likely to prove very valuable in studying the hereditary transmission of pernicious anaemia. Achlorhydria and hypochlorhydria are more common than normal in iron-deficiency anaemia but it is not yet decided which is cause and which is effect. This was a very learned and stimulating address by an authority on gastric function and on diseases of the blood.

After a pleasant but hot summer followed by tremendous activity resulting from the World Medical Association meeting in Montreal, activities in general in our Division are settling down to a normal pace. Dr. D. G. Kinnear has now taken over full responsibilities as the Honorary Secretary of our Division. Plans are also progressing for our next Annual Meeting which will be held for the first time in Quebec City from May 5 to 7, 1960. With a membership of over 1800, the largest ever recorded for our Division, we can look forward to a very active and profitable year.

It is a pleasure to report that Dr. Donald L. McRae, associate professor of radiology at McGill University, was presented with the Caldwell Lecture Medal at the 60th annual meeting of the American Roentgen Ray Society held in Chicago recently. This is given each year in honour of the late Dr. Eugene W. Caldwell, pioneer user of radiation in medicine. Dr. McRae's address was entitled "The significance of abnormalities of the cervical spine".

Dr. George Weber, head of the department of pathological chemistry, Montreal Cancer Institute, has been named director of the new cancer research unit at the University of Indiana's Riley Hospital and also associate professor at the University of Indiana's department of biochemistry and microbiology. Dr. Weber is a graduate in medicine from Queen's University and has been at the Montreal Cancer Institute for the past six years.

It is with great sorrow that your reporter has just heard of the death of Dr. Jonathan Campbell Meakins, internationally renowned physician and teacher, former physician-in-chief at the Royal Victoria Hospital and chairman of the department of medicine, McGill University. This is a great loss to Canadian medicine and a great personal loss of a friend.

A. H. NEUFELD

ABSTRACTS from current literature

MEDICINE

Adenovirus Diseases (in Russian).

E. A. PAKTORIS, L. D. KNYAZEVA AND R. S. DREIZIN:
Klinicheskaya Meditsina, 5: 8, 1959.

The history of adenovirus diseases is reviewed and typical clinical pictures of several patients in whom Type 3 adenovirus was isolated are presented. Although the experience of the authors with these diseases is still limited, certain general characteristics emerge. The disease is most frequent among children and the most common virus is Type 3 adenovirus. The disease caused by this virus is usually characterized by elevated temperature, rhinitis, pharyngitis, conjunctivitis, tonsillitis, scleritis, adenitis and bronchitis. The fever lasts on the average 5-7 days, and the conjunctivitis is usually unilateral and has some significance in the differential diagnosis. In the past the conjunctivitis was probably frequently diagnosed as diphtheria of the eye.

W. GROBIN

Staphylococcal Septicæmia with Recurrent Spontaneous Pneumothorax.

A. SCHWEICH AND J. FIERSTEIN: *Ann. Int. Med.*, 50: 819, 1959.

A case is reported of staphylococcal septicæmia with involvement of the lungs, kidneys and liver and the late development of recurrent spontaneous pneumothorax.

A boy, 14 years of age, was admitted to hospital with fever, cough, bloody sputum, nausea, vomiting, diarrhoea and a macular cutaneous eruption, one week after a febrile pharyngitis. A cardiac murmur, compatible with an intraventricular septal defect, had been noted since early infancy.

Diagnoses considered included rheumatic fever, infectious mononucleosis, enteric fever, penicillin reaction, an infantile exanthem and bacterial endocarditis. Blood cultures, roentgenograms of the chest, tests of hepatic function and urinalyses established the diagnosis of *Staphylococcus aureus* septicæmia with involvement of lungs, kidneys and liver. The possibility of staphylococcal endocarditis could not be excluded. The portal of invasion was probably pharynx or skin. Transmission of a penicillin-resistant staphylococcal infection by a member of the family was a possibility.

Although the organism showed penicillin resistance in a test by the disc method, massive intravenous doses of penicillin were administered to supplement treatment with streptomycin, erythromycin and novobiocin. This combination resulted in cure. Though it was not possible to determine which antibiotic was of decisive importance, reports have been found in the literature of lack of correlation between *in vitro* sensitivity of specific organisms and *in vivo* activity of massive doses of penicillin.

Nodular densities in the chest radiographs developed into annular translucencies. One was situated near the pleural surface of the right upper lobe. A right pneumothorax developed on the 19th day and recurred on the 26th day in hospital. Pneumothorax during the course of the pulmonary infection occurs as the result of necrotizing lesions, of post-infectious pneumatoceles and of subpleural vesicles. In the present case, pneumothorax developed probably as a result of rupture of an abscess cavity in the lung, and empyema was prevented by the antibiotic therapy.

S. J. SHANE

Normal Air Encephalogram in Patients with Tumour of the Brain.R. W. ANGEL AND D. F. BENSON: *Neurology*, 9: 426, 1959.

Brief reference is made to reports from other sources of brain tumours in patients with a normal air encephalogram. In the present series, out of a total of over 140 primary brain tumours eight cases were found in which the initial work was done for suspected brain tumour and a normal "satisfactory" pneumo-encephalogram was obtained. There was in all a latent period of 2-8 years between the first air studies and surgical diagnosis of a brain tumour.

The eight cases are briefly reported and demonstrate clearly that after normal air studies one cannot dismiss the possibility of an expanding intracranial lesion. In seven of the eight patients there was at least one finding in the history, physical examination or electroencephalographic studies which pointed correctly to the diagnosis of a focal lesion. A good response to anticonvulsant drugs should not lead to dismissal of the possibility of brain tumour. The elusiveness of these tumours is not explained on the basis of histological features, as there were three glioblastomas, three astrocytomas, one astroblastoma and one oligodendroglioma among them. Anatomically they involved frontal, parietal and temporal lobes, and six of the eight tumours were located in the dominant left hemisphere.

W. GROBIN

Clearance Rate of Insulin Labelled with I^{131} from Subcutaneous Tissues in Normal and Diabetic Subjects.C. L. JOINER: *Lancet*, 1: 964, 1959.

Since previous examinations of the absorption of insulin from subcutaneous tissues in human subjects were carried out with insulin-4-iodo-azo-benzene, whose biological validity is subject to some doubt, studies were undertaken with a labelled insulin known to undergo no loss in biological activity or immunological reactions. The procedure of labelling the insulin is that of Pearson and is described on page 967 of the same issue of *Lancet*.

The studies were carried out on 59 male and 38 female control subjects and upon 24 male and 17 female diabetic patients. Significant differences were observed in the clearance rates between the arm and the leg in males and females and between males and females in the legs. No marked difference in clearance was found when the volume and the concentration of the injection were varied, nor did exercise increase the clearance rate to any extent. However, the addition of hyaluronidase caused a significant increase in the rate of clearance of labelled insulin. In the 41 diabetic patients the study was preliminary, only the leg being used for injections. The half-period was over 141 minutes in six males and under 141 minutes in 18 males, whereas in the females it was over 111 minutes in nine and under 111 minutes in eight. The slow and fast clearance groups did not differ to any extent as regards diet, distribution of obesity or extent of control, and the only remarkable difference was the duration of the disease. In the diabetics whose disease was of longer duration, clearance of labelled insulin was delayed more frequently than in those with diabetes of shorter duration.

The difference in clearance times in younger and older persons may be explained by assuming that repeated insulin injections over the years may in some way damage the subcutaneous tissues and thus con-

tribute to poorer absorption. In six cases in which absorption was most prolonged from the usual site of injection in the leg, it was restored to nearly normal when the injection was given in the arm. Whilst in some cases delayed absorption may be a significant factor in poor control of diabetes, this was not the case in the present series.

The authors draw three practical conclusions from these studies: (1) When rapid absorption of insulin is important, the insulin should be injected into the arm. (2) Diabetics should vary the site of injection daily. (3) In some cases absorption of insulin may require the addition of hyaluronidase just before injection.

W. GROBIN

Valsalva Manoeuvre as a Diagnostic Aid.C. W. IRVIN, JR.: *J. A. M. A.*, 170: 787, 1959.

When a patient blows into a manometric system and maintains a pressure of 40 mm. Hg for 10 seconds and the blood pressure of the patient is checked during and immediately after this restraining period, a four-phase response is obtained. In the normal this consists of a brief rise, gradual fall to resting level, a brief fall below the original level, and a secondary rise. This Valsalva test was applied to 205 office patients and was found to be simple and, as it does not require any complicated equipment, a practical method to distinguish congestive heart failure from emphysema. Patients with hyperventilation syndrome and psychological dyspnoea were found unable to perform this test satisfactorily. Of the 205 patients who were tested, 35 showed abnormal results. Eight of these patients were thought to have no heart disease; the test was done again and six of them gave a normal response. Some of the patients with normal response to this test were known to have heart disease but were free of congestive heart failure and could thus be reassured of satisfactory compensation. With the exception of one case with aortic stenosis, all patients with valvular heart disease and normal response to the test were judged to be in functional class 1. The author believes that this test should be included in routine examination by every practising physician.

W. GROBIN

Cardiac Chamber Volumes and Their Significance in Rheumatic Heart Disease with Isolated Mitral Stenosis.L. A. SOLOFF AND J. ZATUCHNI: *Circulation*, 19: 269, 1959.

The total capacity of the heart and the volume of each of its chambers were determined by the technique of simultaneous biplane stereoscopic venous angiography in 18 persons with surgically confirmed, isolated severe mitral stenosis. Although cardiac capacity and chamber volumes varied greatly, the left atrium was almost always the largest chamber. The left ventricle was not always the smallest chamber. In fact, it was larger than the right ventricle in seven of the 18, and was the only chamber to be significantly correlated with total cardiac capacity greater than 1000 ml. The right ventricular volume was found to be significantly correlated with its systolic pressure, or with the pulmonary artery systolic or mean pressures. It is clear, therefore, that disproportionate enlargement of the right atrium can occur in the absence of tricuspid stenosis. Finally, atrial fibrillation was commonly present in patients with a large total cardiac capacity.

S. J. SHANE

Staphylococcic Pneumonia.

S. EDE, G. M. DAVIS AND F. H. HOLMES: *J. A. M. A.*, 170: 638, 1959.

Of 1177 patients with acute pneumonia (10% of all admissions to a U.S. Naval Hospital in 1957-1958) 18 cases (1.5%) were due to a staphylococcus. In 1956-1957, the percentage was the same although the total number of cases of acute pneumonia was less. In the 36 cases of staphylococcic pneumonia observed during the past three years the following complications were found: death, one; bilateral pyopneumothorax, one; unilateral pyopneumothorax, eight; pleural effusion, eight; empyema, ten; lung abscess, three; pericarditis, one; shift and fixation of mediastinum, one; pneumatocele, one; and atelectasis, two. Thoracentesis was performed in 16 cases, thoracotomy with closed tube drainage in 15, partial lobectomy in one, and decortication in three. Most of these cases were not due to a "hospital organism". Although nothing short of bacteriological proof definitely identifies the disease, several significant findings should alert the clinician to the possibility of staphylococcic pneumonia. They are: (1) dyspnoea out of proportion to physical findings; (2) dusky cyanosis with dyspnoea in the more virulent forms; (3) normal findings or minimal involvement in the chest radiograph for the first 24-48 hours. Empyema secondary to acute pneumonia, rapid involvement of the entire hemithorax, the development of pyopneumothorax or a bronchopleural fistula during acute pneumonia almost confirms its staphylococcal origin. The authors found that disc-sensitivity was practical and useful for determining appropriate antibiotics. Penicillin and tetracyclines gave satisfactory results in some of these infections but in severe cases a combination of chloramphenicol with erythromycin and of novobiocin with erythromycin was the most reliable. Therapy was continued for 7-10 days after apparent recovery. Close co-operation between surgeon and internist is necessary and when complications arise prompt surgical intervention is advisable.

W. GROBIN

Adrenal Insufficiency After Gastrectomy (in French).

J. SCHWARTZ AND M. SIMLER: *Schweiz. med. Wchnschr.*, 89: 529, 1959.

This study is concerned with 132 patients admitted to hospital during the past two years because of disorders attributable to gastrectomy. Except for one patient whose gastrectomy had been performed five months before admission all operations had taken place on an average seven years previously (2-18 years). The most frequent finding in this series was a considerable loss of weight. The 17-ketosteroids and dehydro-iso-androsterone values and the ACTH test response were investigated in 54 patients whose nutritional status was particularly reduced. In 85% of these cases, the level of urinary 17-ketosteroids was reduced. In two cases out of three with clinical signs of adrenal insufficiency, the ACTH test result was abnormal, confirming the diagnosis of primary adrenal insufficiency. The authors conclude from their investigations that the adrenal insufficiency is mainly a result of failure of pituitary stimulation, which in its turn ensues from malnutrition. Prolonged failure of pituitary stimulation of the adrenal may in some cases result in irreversible and definite adrenal insufficiency, i.e. Addison's disease.

W. GROBIN

SURGERY

Atrial Septal Defect, Secundum.

H. SWAN *et al.*: *J. Thoracic Surg.*, 37: 52, 1959.

In 100 consecutive cases of atrial septal defect secundum seen at open-heart surgery, there were seven operative deaths among the first 43 patients and none among the last 57. The natural history of the disease, diagnostic criteria, and indications for surgery are discussed. The authors urge that, in the light of the safety of the operative procedure described, all patients with this diagnosis should be given the benefit of surgical repair unless the pulmonary resistance is greatly elevated.

The operative techniques employed to meet the various anatomical variations encountered are described. This group considers that hypothermia is now the method of choice in performance of these operations.

The current status of all but one of the surviving patients is known, and most are cured by all means of assessment; three are improved but still have some symptoms; three have small residual shunts which do not seem to be of haemodynamic significance; one patient has become cyanotic as a result of the passage of inferior vena caval blood into the left atrium; one patient has persistent pulmonary hypertension after closure of the defect; and two patients have residual shunts of sufficient degree to warrant a second intervention.

The authors consider that atrial septal defect of the "secundum" type is a congenital malformation which can be diagnosed clinically with great accuracy and which can be successfully treated surgically by open operation during hypothermia at a very low risk. Operation should be performed on all patients with this disease during childhood, as soon as convenient after the diagnosis is made.

S. J. SHANE

Massively Bleeding Duodenal Ulcer with Special Reference to the Crater.

B. GARDNER AND I. D. BARONOFKY: *Surgery*, 45: 389, 1959.

The authors, from the Mount Sinai Hospital in New York, use as their criterion of massive bleeding a haemoglobin level of less than 8.0 g. per 100 ml. and a history of bleeding within the previous week, followed by collapse. In 1087 cases of duodenal ulcer, 235 massively bleeding ulcers were found. In this group, the older patients did not appear more likely to bleed massively. Of the patients with massively bleeding ulcers, 188 were treated purely medically at first. Of the 47 patients who remain, three died. One of these was a child who had an exploration which did not reveal the cause of the bleeding. At autopsy, an acute duodenal ulcer was found eroding the superior pancreaticoduodenal artery. The second fatality occurred when the base of the ulcer was left *in situ* and it continued to bleed. The third patient had a cardiac arrest on the operating table and died 17 days after operation.

The authors feel that if vagotomy and gastroenterostomy have a place in the treatment of bleeding ulcer, it must be accompanied by ligation of the bleeding point in the ulcer.

Radiographs of the gastro-intestinal tract were usually taken after the patients' condition had stabilized and they had guaiac-negative stools. Craters are considered by the radiologist to indicate the persistent presence of a localized, rounded collection of barium. The presence of such a crater on x-ray examination indicates that the ulcer has penetrated into submucosa or muscle.

A crater was a more constant finding in the groups with more severe bleeding. It was also found to be of prognostic value, in that those patients (with craters) were more likely to have recurrent bleeding and to require subsequent operation.

Medical treatment is the initial choice in all bleeding duodenal ulcers. Operation should be considered if a patient needs more than 2000 c.c. of blood in less than 24 hours to maintain blood pressure, or if a patient is still bleeding after 48 hours.

Subtotal gastrectomy is the procedure of choice. The involved vessel should be ligated where possible. An added vagotomy may be helpful.

Posterior wall ulcers are the most dangerous with regard to bleeding. The persistent pain due to penetration into the pancreas is a bad prognostic sign. If the patient is not in shock or actively vomiting, emergency roentgenological examination can be carried out. Duodenal ulcers can be diagnosed on radiographs taken during active bleeding. Craters can be demonstrated without palpation or compression.

The presence of a crater late in the course of a medically treated bleeding duodenal ulcer indicates some intractability and may be an indication for early surgical therapy.

Follow-up of patients treated medically revealed that when no crater was demonstrated during the hospital stay for the bleeding episode, the incidence of recurrent bleeding was 40%. When a crater was demonstrated during hospital stay, bleeding recurred in 72.5% of the patients.

Follow-up on medically treated patients revealed an incidence of subsequent operation in 26.7% if no crater was demonstrated and 60% if a crater was demonstrated.

It is suggested that patients with acute massive hæmorrhage due to duodenal ulcer be operated upon much sooner when a crater is demonstrated roentgenologically.

T. A. McLENNAN

Tracheo-oesophageal Fistula after Closed Trauma to the Thorax (in French).

P. SANTY *et al.*: *Lyon Chir.*, 55: 5, 1959.

The first successful operation for traumatic tracheo-oesophageal fistula was performed by Adams and Mathey in 1946, and the present authors report the eleventh case of this condition in the world literature. It is the eighth case treated surgically and the seventh to survive.

The diagnosis is suspected after any severe thoracic injury. Hæmorrhage, if severe, may cause immediate death. In cases that survive, the earliest sign may be regurgitation of saliva—as is found in the congenital type. Within two to three days, dysphagia begins. The taking of liquid foods is eventually followed by spells of coughing and choking. This suggests that it takes several days for the fistula to develop. When it occurs, cervical emphysema is almost diagnostic of the condition. If a fistula develops, pulmonary infection or infec-

tion of the mediastinum may occur. Radiographs may show a pneumothorax due to tracheal rupture.

The diagnosis is made by bronchoscopy and oesophagoscopy in some cases. It is confirmed by iodized oil swallow examination in preference to using barium. The usual site of rupture of the trachea is at 24 cm. from the incisor teeth—just above the carina. The defect is usually easily seen and is about 1 to 3 cm. long and 0.5 to 1 cm. wide. With respiration, bubbles of air will be seen to move the small patches of mucus around the defect. Inflammatory changes may be evident. When bronchoscopy alone is carried out, the oesophagus may be visible through the defect, using a right-angled telescope.

It is believed that tracheal rupture is the primary cause of the condition. Infection at the site may lead to adherence of the oesophagus with eventual fistula formation.

Preoperative care includes adequate antibiotic preparation, a Levin tube for feeding purposes and on occasion a gastrostomy if the patient has been poorly nourished. Operation should be carried out as soon as is commensurate with the patient's welfare.

Anæsthesia includes use of a cuffed endotracheal tube situated so as to occlude or bypass the hole in the trachea. The approach is preferably by a right lateral thoracotomy through the 4th or 5th space, although the face-down position mentioned by Lockwood is noted. At operation, the azygos vein is divided and the mediastinal pleura opened. The oesophagus is mobilized and the fistula dissected free. The fistula is divided and the tracheal opening closed first with interrupted nylon. The oesophagus is then closed with two layers of interrupted silk. The mediastinal pleura is left open and a drain inserted in the right chest.

The Levin tube is left in for several days. In the author's case the gastrostomy required a secondary closure.

T. A. McLENNAN

Routine Cardiac Monitoring During Surgery and a Cardiac Arrest Team in a General Hospital.

V. PARSONNET AND A. BERNSTEIN: *A.M.A. Arch. Surg.*, 78: 393, 1959.

The mortality rate of cardiac arrest appears to be about 70%. Half the cases occur in patients with apparently normal hearts and all should recover, though only 20% of patients with heart disease survive. The difficulty in making the diagnosis early enough to start cardiac massage within the necessary three or four minutes is the probable reason why only 30% survive.

At the Newark Beth Israel Hospital, there is a program of yearly lectures and animal demonstrations, plus a house-staff cardiac arrest team with a paging system, plus a cardiac monitor-alarm in each operating room, cystoscopy room and recovery room. The monitor used has an alarm that sounds at the cessation of cardiac activity and a single chest strap for electrodes. It is attached to every patient undergoing general anæsthesia.

Besides a great improvement in the survival of cases of cardiac arrest since instituting this program, there have been fewer cases, for anæsthetists and surgeons spend more thought and time correcting unfavourable factors such as anoxia, excessive sedation, anæmia or electrolyte imbalance. In the latest case of arrest, the chest was open within 20 seconds of standstill.

BURNS PLEWES

THERAPEUTICS

Atrial Flutter as a Manifestation of Digitalis Toxicity.

J. D. COFFMAN AND G. H. WHIPPLE: *Circulation*, 19: 188, 1959.

Atrial flutter is a rare complication of digitalis intoxication. The authors could find only 15 definite cases in the literature. A 16th case of atrial flutter due to digitalis toxicity is presented in this paper. The patient was an elderly man in severe congestive heart failure who had received 7.25 mg. of digoxin during a nine-day period.

Digitalis as a cause of atrial flutter should be suspected when the arrhythmia is associated with ventricular premature beats, despite a rapid ventricular rate, if congestive heart failure is not marked. The same may be said of flutter that develops in the presence of a slow ventricular rate in a heavily digitalized patient with congestive failure. A therapeutic trial of potassium may be helpful in doubtful cases.

S. J. SHANE

Effects of Chlorothiazide on Specific Renal Functions in Hypertension.

A. C. CORCORAN *et al.*: *Circulation*, 19: 355, 1959.

The information contained in this paper demonstrates that, in addition to its recognized saluretic and kaliuretic properties, prolonged oral administration of chlorothiazide to hypertensive patients often depresses glomerular filtration, causes an increase in blood urea that may be disproportionate, and even in the face of decreased filtered sodium load, tends to maintain a normal rate of sodium reabsorption. It also causes an increase in free water reabsorption, only relatively evident in prolonged experiments but observed as an absolute increase in tests shortly after intravenous injection of the drug. The renal haemodynamic status during prolonged administration may be attributable to sodium depletion. However, by analogy with renal haemodynamic status in nephrosis, hypovolaemia may be the primary factor.

S. J. SHANE

Developments in Fibrinolytic Therapy for Thrombo-embolic Disease.

S. SHERRY, A. P. FLETCHER AND N. ALKJAERSIG: *Ann. Int. Med.*, 50: 560, 1959.

The presence of the precursor of a fibrinolytic enzyme in human plasma supports the concept that enzymatic fibrinolysis is an important physiological mechanism to rid the organism of intravascular thrombi. As a result, several groups of investigators have occupied themselves in attempting to develop a direct form of therapy in cases of human thrombo-embolic disease by regulating fibrinolytic activity in the circulation. At the present time, interest is concentrated primarily in the use of partially purified preparations of human fibrinolysin or of naturally occurring activators of fibrinolytic enzyme systems.

The present report is a review of the components of the system of enzymatic fibrinolysis in humans, of recent studies relative to the mechanism which brings about lysis of thrombi, and of the application of this information to the production of a regulated fibrinolytic state in the human circulation. The current status of these studies as they concern the therapy of thrombo-embolic disease is discussed.

S. J. SHANE

Comparative Effectiveness of Phenylpropanolamine and Dextro-Amphetamine in Weight Reduction.

J. F. FAZEKAS *et al.*: *J. A. M. A.*, 170: 1018, 1959.

This study was carried out on 80 mentally deficient obese patients who had been residents of an institution for a number of years. They were divided into four approximately equal groups, and each subject was given a preparation which was unknown to the supervisors who administered them. After the completion of the study it was disclosed that one group received 25 mg. of phenylpropanolamine three times a day, the second group received 50 mg. of this drug three times a day, the third group received 5 mg. dextro-amphetamine and the fourth group a placebo. All the drugs and the placebo were administered in capsule form and were indistinguishable. The results obtained with regard to weight reduction are tabulated for each of the four groups and it is apparent that no significant difference was observed between the groups on phenylpropanolamine and the one on the placebo. Neither of these groups achieved any marked weight loss, whilst the mean weight loss for the patients on dextro-amphetamine was 4.6 lb. Whilst it is possible that phenylpropanolamine may be useful as an anorexic agent in receptive or susceptible people, it has not the same appetite-reducing effect on the central nervous system as amphetamine.

W. GROBIN

Intracranial Haemorrhage as a Complication of Anticoagulant Therapy.

K. D. BARRON AND G. FERGUSSON: *Neurology*, 9: 447, 1959.

Anticoagulant therapy was associated with intracranial haemorrhage in five cases. Two patients were hypertensive and two patients had embolic infarcts for which anticoagulant therapy was being administered. In all five, the prothrombin time was 35-45 seconds on the day of death and in at least three patients anticoagulants were believed to be the ultimate cause of intracranial haemorrhage. An addendum mentions a case of fatal haemorrhage in a hypertensive male on dicoumarol whose prothrombin time was 21 seconds (control time 11). Literature on the subject is reviewed and caution advised in the use of anticoagulants in hypertensives or in patients with recent cerebral infarcts.

W. GROBIN

DERMATOLOGY

Erythema Nodosum

C. M. R. VESEY AND D. S. WILKINSON: *Brit. J. Dermat.*, 71: 139, 1959.

This is an analysis of 70 consecutive cases of erythema nodosum. Thirty-two were proven or presumed streptococcal in origin, 25 accompanied sarcoidosis, nine were mixed or of unknown origin and four were tuberculous. The nodules occurred mainly on the front of the legs and thighs, were multiple and tender and measured from 0.5-2 cm. in diameter. A bruise-colour occurred during fading. The duration of the attack was from 3-8 weeks. The authors stress the importance of distinguishing erythema nodosum from such diseases as nodular vasculitis, thrombophlebitis migrans, *Trichophyton rubrum* granuloma and recurrent erysipelas.

ROBERT JACKSON

Penicillinase Therapy — Clinical Report of Severe Reactions.M. REISCH: *J. A. M. A.*, 169: 594, 1959.

The author reports two cases of severe reactions following the use of penicillinase in the treatment of drug eruptions due to penicillin. In both cases the reaction from the penicillinase was much worse than the penicillin drug eruption.

ROBERT JACKSON

Hula-Hoop DermatitisI. N. HOLTZMAN: *A.M.A. Arch. Dermat.*, 79: 590, 1959.

A 4-year-old girl developed an itching papulovesicular eruption on the palms and ventral surfaces of the fingers. The clinical impression was of contact dermatitis. Patch tests from scrapings of plastic material from three different coloured hoops showed an erythematous papular reaction in 48 hours. The eruption improved with the use of topical steroids and the avoidance of plastic hula-hoops. The patient now uses an aluminium hoop.

ROBERT JACKSON

PÆDIATRICS**False "Coronary Patterns" in the Infant Electrocardiogram.**P. DOMINGUEZ, B. L. LENDRUM AND A. PICK: *Circulation*, 19: 409, 1959.

Electrocardiograms of five infants with characteristic changes of severe acute injury, imitating patterns of acute myocardial infarction, were analyzed. In four of the cases abnormality of the coronary blood supply could be ruled out by autopsy, and in one it was thought to be excluded on clinical grounds. In three the changes were attributable to acute diffuse myocarditis, and in two to unusual digitalis effects.

A comparison with similar previously reported electrocardiograms in infants, in which the etiological factor could be ascertained by autopsy, suggests that "coronary" patterns in infancy are of "true and false" types. The true variety, caused by a congenital or acquired disorder of coronary blood supply to the myocardium, is associated with a pattern of anterior or antero-lateral wall infarction. In the false variety either an anterior or posterior wall pattern may be found. The commonest cause of a false coronary pattern in an infant appears to be an acute diffuse myocarditis.

S. J. SHANE

INDUSTRIAL MEDICINE**Visual Comfort in the Plant.**W. H. KAHLER: *Indust. Med.*, 27: 556, 1958.

People perform most effectively when their surroundings are comfortable, pleasant, and geared to easy visual perception. Progressive factory planners recognize the significance of the "luminous environment", which comprises: (1) brightness from lighting fixtures; (2) brightness (daytime) from windows, skylights, etc.; (3) reflected light from floor, walls, ceiling and equipment.

Direct glare will cause discomfort, annoyance, interference with vision and eye fatigue. Industrial lighting fixtures with upward components lead to a more comfortable and more cheerful environment. Other factors contributing to greater visual comfort are: light-coloured finishes on the outside of lighting fixtures,

higher mounting heights, and better shielding of the light source by deeper reflectors, cross baffles, or louvres.

All brightnesses in the field of view should be carefully controlled. A practical guide to recommended maximum brightness ratios for industrial areas is presented in a table. To provide the recommended brightness relationships and high utilization of light, high reflectance surfaces are generally desirable. Recommended reflectance values for industrial interiors, furniture, machines and equipment are given as follows: ceiling 80%, walls 60%, desk and bench tops 35%, machines and equipment 25 to 30%, and floors not less than 15%.

In manufacturing processes, glare caused by reflection of high brightness light sources from shiny surfaces may be a particularly serious problem. It can be minimized or eliminated by using low brightness light sources or by orienting the work so that reflections are not directed to the normal line of vision.

The colour of light should be carefully selected where colour discrimination or colour matching are a part of the work process. For example, in the printing industry a standard colour of light for appraisal of colour work has been created by the industry and the Illuminating Engineering Society.

MARGARET H. WILTON

Occupational Dermatoses—an Introduction.COUNCIL ON INDUSTRIAL HEALTH: *J. A. M. A.*, 167: 1636, 1958.

Occupational diseases of the skin constitute the major portion of all compensated illness of industrial origin. Their continuing importance may be anticipated in view of the increased number of workers in industry and the more widespread use of chemical processes. New chemicals are constantly being introduced, particularly those incidental to contact with plastics (synthetic resins), petroleum products, and synthetic materials from petroleum and coal tar.

Available statistics emphasize the importance of this disease. In a study made in 1951, occupational disease statistics gathered by the U.S. Public Health Service from 28 states showed that dermatoses constituted approximately 55% of all occupational diseases reported. They indicate also the importance to industrial physicians of an adequate knowledge of dermatology, and the importance to dermatologists of knowledge concerning the nature and hazards of occupational activities in relation to effects on the skin.

The causes of industrial dermatoses included chemicals, physical agents, mechanical factors, bacteria and fungi, animal parasites, plants and woods. In industrialized areas, about 90%, excluding mechanical injuries, are of chemical origin; these cases are of greater importance because of their severity, difficulty of management, and frequently disabling character. Although sensitizing agents cause no more than 20% of the cases, these dermatoses require experienced dermatological knowledge for correct diagnosis and successful management.

Appreciation of preventive measures, together with education of employees and improvement in plant operations and procedures, lessens the incidence of occupational skin disease. The handling and correction of sensitization dermatoses is more difficult, requiring greater care, and if practicable, replacement of the sensitizer by a nonsensitizing material.

MARGARET H. WILTON

BOOK REVIEWS

NOTES OF A SOVIET DOCTOR. G. S. Pondoev, Honoured Physician of the Georgian U.S.S.R. Translated from the Russian by I. Galdston. 238 pp. Illust. Consultants Bureau, Inc., New York, 1959. \$4.95.

The author dedicates this book to young Soviet doctors about to enter medical practice. For the uninformed reader, it would create a picture of medicine in the Soviet Union which is much more nearly ideal than that in the West. Soviet medicine is glorified, and the shortcomings, both existent and non-existent, of the "bourgeois" medical system are emphasized throughout this book. It would be easy to dismiss this book as propaganda, but in spite of such aberrations it does reflect the personal experience of a doctor who has been practising for 50 years. Even continuous political indoctrination could not destroy the great love for humanity in this old and true physician. It is a pity that little, if any, mention is made of the shortcomings facing the young Soviet doctor about to start out on his own. As private practice is officially non-existent, it should have been easy to outline various careers open to him and to point to their various problems. However, nothing except generalizations about "glorious" Soviet medicine and Soviet doctors is presented.

Much of the useful advice given when put into simple "non-dialectic" language can be found in any of the orations rendered to graduating classes in the "bourgeois" world. On the other hand, it is disturbing to find the admonition that the doctor is to execute strictly all the demands of the public health authorities. "It goes without saying that disobedience to them entails punishment according to the existing laws, as well as censure of the community, including the medical community." It is obvious that anybody practising medicine in the Soviet Union today must be familiar with Marxist-Leninist theories (for self-protection, if nothing else), but it is doubtful whether this would necessarily produce better medical practice. His concept of medicine as practised in the West is, to say the least, very naïve. That students have to be admonished to learn how to do cupping, give enemas and apply leeches is most illuminating.

As can be expected, a great deal of praise is lavished on Pavlov and his school and their influence on Soviet medicine. The discovery of the close relationship of body and mind by Russian doctors is given great prominence, and the indivisibility of those two is stressed. "What exists as a single entity must not be treated separately."

In his introduction to this translation, Iago Galdston says that Pondoev has three distinctive personalities—"urbane, well-read and broadly experienced doctor whose counterpart is to be found among the best . . . A doctrinaire who pontificates a straight line orthodoxy; and an illuminated humanist who is committed to—and endeavouring to communicate with professional successors—man's aspirations for the true, the good and the beautiful . . . The odd part is that the three seemingly never meet, have no awareness of one another, are, so to say, co-existent without recognition."

This may well be the reason for much that is strange to us about this book in particular and about Soviet medicine in general. For those interested in knowing what leading physicians in Soviet Russia write about their work, this book is most useful.

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THE TREATMENT OF DIABETES MELLITUS. Elliot P. Joslin and others. 798 pp. Illust. 10th ed. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1959. \$16.50.

This book was first published in 1916, has been continuously revised since then, and had its previous edition in 1952. An authoritative treatise dealing with every aspect of diabetes, it includes in its present edition a very extensive appraisal of oral hypoglycaemic agents. The whole book is physically not unlike its predecessors, having added only some 20 pages to the total; many chapters have been brought up to date as regards theory and practice in various aspects of diabetes. All the statistics of long-term outcome of treatment of diabetes, survival rates, incidence of coma, etc., are brought up to date as well.

Most of the chapters, especially the clinical ones, are pleasant to read, and one wonders whether they have not been made somewhat too easy. The opportunity to read first-hand the distilled experience of the master in the chapters by Joslin is in itself of the utmost value. They demonstrate not only the art and science of diabetes, but also the art of describing and presenting it lucidly and simply. The chapter on physiology of diabetes mellitus by Renold is remarkably up-to-date, 1958 literature being quoted. There is an extensive bibliography appendix to all the chapters, which in itself makes the book valuable as a reference source for research workers. Alice Marble wrote the chapters on applied physiology and on oral drugs. The latter is, of course, not inclusive of the latest drugs which have become available but deals authoritatively with the most important oral hypoglycaemic agents. One can sense in the whole book the reflection of the observation by Marble that

the introduction of oral hypoglycaemic agents has not only brought considerable improvement in the management of certain types of diabetes, but has also stimulated research into the nature of this disorder. All in all, this is a delightful book of great value to the student and the young research worker in diabetes and a valuable reference book to the diabetic specialist.

This reviewer was interested in the chapter on the digestive system in diabetes and the relationship between ulcer and diabetes mellitus. It has been suggested in the past that the two diseases are incompatible and the question arises whether peptic ulcer in diabetics is a form hitherto neglected and differing in etiology from other forms of peptic ulcer. One could have wished for more emphasis on the difficulties encountered in the dietetic treatment of diabetics who also have a peptic ulcer. There is no undue increase of malignant disease in diabetics, but cancer of the pancreas, by contrast, was found to comprise some 13% of all cases of malignant disease in diabetics (compared with 4.5% in the general population). Many other chapters could be mentioned as deserving special praise. There is, for instance, the well-known chapter by Priscilla White on pregnancy complicating diabetes and the first chapter by Joslin on the present concepts of diabetes. As in previous editions, the experience of the Joslin clinic with increasing numbers of diabetics who have survived more than 25 years is a source of moral support to any doctor treating large numbers of diabetics and becoming discouraged by lack of success in controlling their diet and weight.

Except for a few typographical errors, including one in the title of a chapter (p. 299), the printing is good.

MODERN CHEMOTHERAPY OF TUBERCULOSIS. Antibiotics Monographs No. 11. Roger S. Mitchell and J. Carroll Bell. 109 pp. Illust. Medical Encyclopedia, Inc., New York, 1958. \$4.00.

This little book of only 80 pages contains an astonishing amount of information useful to any physician supervising chemotherapy for tuberculosis. Anyone who has heard Roger Mitchell's presentations at medical meetings will not be surprised at the clarity of the material presented here. The associate author, Dr. Bell, completes the picture with his presentation of the laboratory basis for antituberculosis chemotherapy. The book begins with a brief history of the better-known antituberculosis agents, before considering their pharmacology, modes of action and dosage. While the chapter on pharmacology makes rather heavy reading for anyone but an organic chemist, some idea of this aspect of the subject is necessary for anyone wishing to understand the subject adequately. The chapter on modes of action is short but adequate and suggests additional reading for anyone wishing to probe more deeply.

The whole subject of dosage and of chemotherapeutic regimens produces great argument whenever specialists in this subject meet, and prevailing opinions are presented most fairly. There is probably room for argument with some of the conclusions reached, as the authors indicate they expect. For instance, at least some studies give a higher rate of drug resistance found in first treatment cases than does Dr. Mitchell. This is to be expected, however, as some studies divided into age and sex show a considerable variation in the incidence of resistance in different groupings.

Any tuberculosis specialist will find the book most interesting and stimulating and the bibliography of some 510 entries should give ample support for these statements presented by Drs. Mitchell and Bell. Another group of physicians who will find the book invaluable are those general practitioners who are more and more called upon to continue chemotherapy or even to institute it. They will find here the information they require regarding dosage, treatment regimen, duration of treatment, and side effects and their relative importance. Some side effects are trivial and some extremely dangerous, while the great variety is confusing to anyone who may be treating only a few cases. It would seem essential for anyone undertaking to treat these cases outside of hospital to study this book thoroughly before commencing treatment, so that he will be able to handle situations that otherwise might be quite disturbing. For anyone treating tuberculosis, the book is most useful and for those who have not been able to keep up with the current specialized literature, it is essential.

INSTRUMENTATION IN ANESTHESIOLOGY. William H. L. Dornette, University of Tennessee College of Medicine, and Verne L. Brechner, University of California School of Medicine. 242 pp. Illust. Lea & Febiger, Philadelphia; The Macmillan Company of Canada Limited, Toronto, 1959. \$8.00.

The authors have prepared an interesting, instructive and timely book about instruments used in anaesthesia by the clinician and the investigator. Instruments improve perception and record some facts our senses cannot appreciate. Monitoring devices must not endanger the patient in any way, but sometimes the lack of such instruments may be hazardous.

The early chapters review clearly elementary physics, leading to descriptions of electrocardiography, electroencephalography, thermometry, manometry, and fluid flow measurement with many diagrams and pictures. The Ploss stethoscope with moulded earpiece is the only instrument which the authors specifically state should belong to every anaesthetist. There are chapters on gas analysis.

Methods of using the apparatus are given in detail; difficulties are mentioned, with means of avoiding and rectifying them. There is a discussion about choice of equipment for the purchaser.

Sections of this volume could be read profitably by all anaesthetists. Other parts are more specialized but should be useful and informative.

MEDICAL LABORATORY INVESTIGATIONS. Ian Dawson and William Goldie. 259 pp. Butterworth & Co. (Canada) Ltd., Toronto, 1958. \$7.00.

This book might be considered as a handbook of medical laboratory investigations. Most of the hospital laboratory fields are covered so that, of necessity, the information about any one test is scanty. The authors claim to be writing for the clinician, the houseman and the medical student, but the reviewer wonders whether the book might not serve best as a reference book of laboratory procedures at the nurse's level. The chapter on morbid anatomy and histology would probably not find favour with Canadian pathologists, but the information given in the other chapters appears to be accurate. The book is not and does not claim to be written for the laboratory or the laboratory worker.

TRIGEMINAL NEURALGIA. Byron Stookey and Joseph Ransohoff. 366 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1959. \$11.75.

This monograph is based upon Dr. Stookey's experience with some 700 patients suffering from trigeminal neuralgia and treated by him at the Presbyterian Hospital in New York City. The account of this experience is preceded by a review of the history of our knowledge of the condition and of the embryology, anatomy and physiology of the fifth nerve.

Some account is given of the clinical features of trigeminal neuralgia and of other causes of pain in the face and neck, including the management of herpes zoster. The bulk (almost two-thirds) of the book is devoted to a discussion of the various forms of treatment of trigeminal neuralgia.

The authors are strong and persuasive advocates of the operation of subtemporal trigeminal dorsal root section as the treatment of choice. They dismiss other forms of treatment as unsatisfactory or dangerous or both. This accords with the current practice in most centres, save those in which alcohol injection of the gasserian ganglion is practised by one specially skilled and experienced in the procedure. The figures reported by the authors—87% of patients permanently cured, a mortality rate of 0.82% and an uncomplicated postoperative course in 82%—testify to their success. Serious and lasting postoperative complications seem to have been uncommon, and troublesome postoperative paræsthesiæ occurred in about 10% of patients.

The book is factual and detailed but the reader is rewarded by occasional tid-bits, such as the news that trigeminal neuralgia, as a clinical entity, was first described in a work called "Practical Observations on Diseases of the Urethra", published with the "approbation of the King".

The book is excellently produced. It contains a great deal of detailed information about the field with which it deals and will be of corresponding value to those who see many cases of trigeminal neuralgia. A wider discussion of the whole subject of facial pain would have given the book a more general interest.

LONGITUDINAL STUDIES OF CHILD PERSONALITY. Alan A. Stone and Gloria Cochrane Onqué. 313 pp. Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders and Company Limited, Toronto, 1959. \$5.50.

This volume is the result of abstracting activity of two Yale medical students. It represents the groundwork for a research project of Milton Senn and Ernst Kris, of the Yale University Child Study Center. It covers the period from pregnancy to adolescence and contains some 297 abstracts of the literature from the twenties until 1955.

The quality of the abstracts is bald but good, and the range wide. The subject coverage is sparse and there are no references to the size or quality of the bibliographies or the articles reviewed. The book will therefore be of most use for those who wish minimal information or who will make it a starting point for more intensive inquiry. As one who has always been extremely impressed by the seemingly endless productivity of child psychiatrists and psychologists, this reviewer is surprised to see the bulk of 30 years of productivity reduced to a small volume. One is also surprised to see how very few productive studies are completed over a long period of time. This is particu-

larly important in child psychiatry where one is attempting to determine whether the earnest activity of the child study unit workers is related, in any way, to the achievements and mental health of their patients in later life.

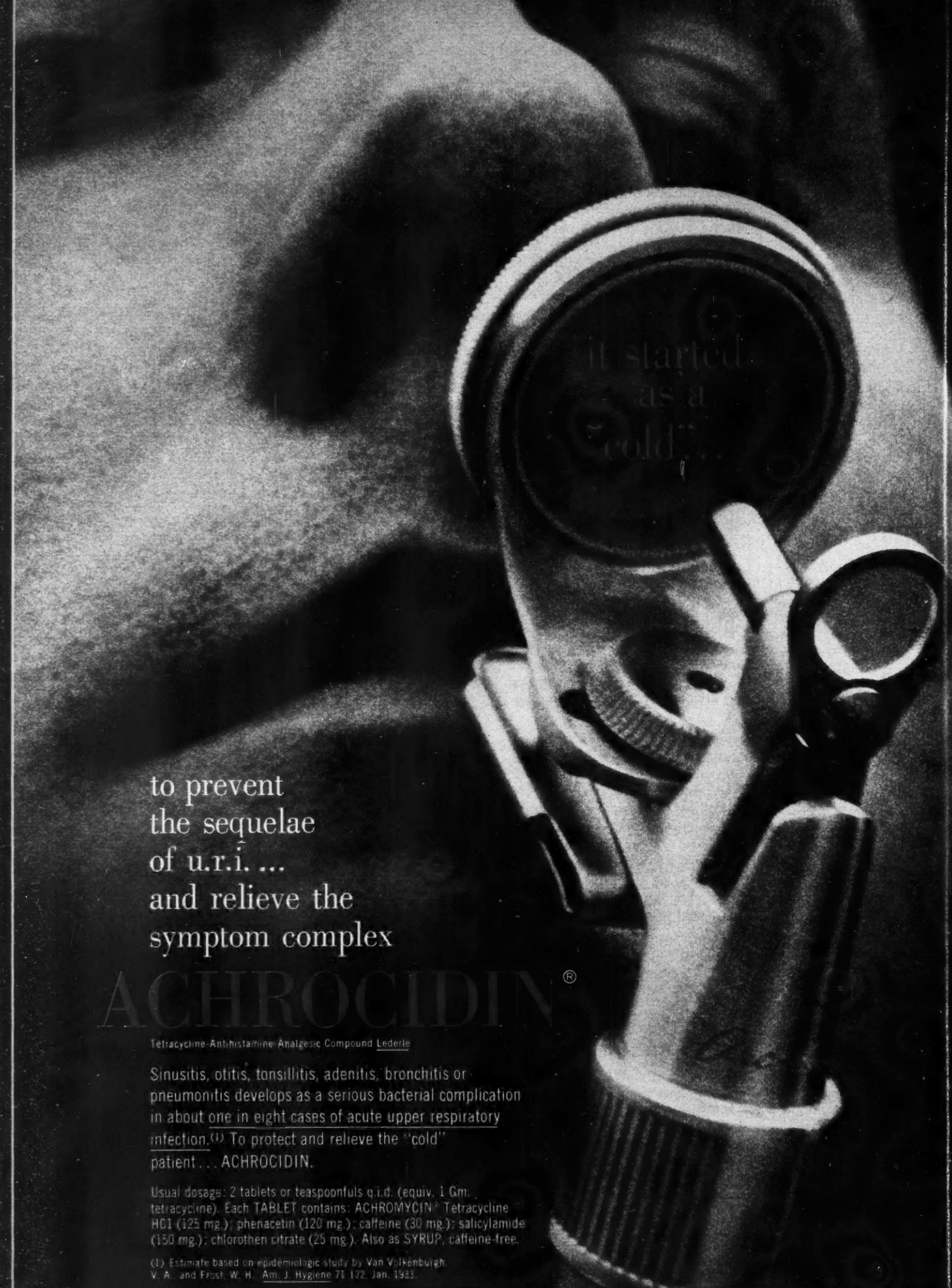
The answer to this question will not be found in this volume, since the time span, as stated explicitly in the text, is only rarely as long as 10 years (e.g. Paulsen and Newman, Freeman and Holzinger) and usually much less, sometimes being discreetly left unstated by the original authors.

The volume is then a good source book for the literature of child study. Its technique is mechanical, e.g., the authors have not written the original authors to remedy defects in the reporting of original papers. Also the order of articles is determined alphabetically by the first letter of the first author's summary. The index, which one would expect in a volume such as this to be at least one-quarter the length of the subject matter, occupies only 17 pages. However, the volume is readable and well printed and will serve a useful function, covering the nascent years of child study. One only wishes that the energies of more medical students would come to such useful fruition.

PSYCHIATRISCHE UND NERVENKLINIK. KRANKENVORSTELLUNGEN (Psychiatric and Neurological Clinics. Case Presentations). Kurt Kolle. 252 pp. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1959. \$4.70.

The author is professor of neuropsychiatry at the University of Munich, and the successor of Kraepelin and Bumke, leading figures in the field of psychiatry and neurology in Germany. In addition to Kraepelin's well-known classification of psychiatric diseases, Kolle endeavours to teach psychopathology. To him (and according to Jaspers' definition) psychopathology is a "methodically arranged science of the abnormal psychic life", i.e. the endeavour to gain a clear view of what the physician observes in his patient. However, this endeavour remains strictly on the surface, which is not even scratched, and not the slightest attempt is made to make the undergraduate medical student acquainted at least with some basic knowledge of psychodynamics and deep psychological processes taught by any of the acknowledged schools. From this viewpoint the type of psychiatry presented appears outdated and of little value for the teaching of psychiatry these days. However, this book might be quite interesting for psychiatrists who are teaching psychiatry in medical schools and who have had no opportunities to see how the specialty of neuropsychiatry is taught in most schools in the German-speaking countries (Germany, Austria and Switzerland), although some of these schools are of course making serious efforts at modernizing their teaching. Here several selected patients are presented by the professor himself for an average of five hours weekly during two semesters; he comments on the presented cases and adds his theoretical teaching, using all sorts of didactic material. This is the main source of information and stimulus for the medical students. This book, which makes no claim to be a textbook, is based on stenographic records of many case presentations covering a wide range of various psychiatric and some neurological conditions.

(Continued on page 871)



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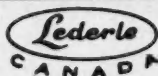
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(1) Estimate based on epidemiologic study by Van Volkenburgh, V. A. and Frost, W. H. Am. J. Hygiene 71: 122, Jan. 1933.

MEDICAL PRODUCTS DEPARTMENT



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(Continued from page 869)

ASEXUALIZATION. Johan Bremer, Gaustad Mental Hospital, Oslo. 366 pp. The Macmillan Company, New York; Brett-Macmillan Ltd., Toronto, 1959. \$5.00.

There has been a need for a review of the results of legal castration. Whenever a sex offence is committed in a community, this "therapeutic approach" is usually loudly recommended by a punitive public opinion. Although the clinician might have strong feelings that this procedure would not serve the intended purpose, it has often been difficult to substantiate this opinion by reference to case studies. In this work Dr. Bremer reviews previous follow-up studies of sex offenders treated by means of legal castration in Switzerland, Denmark, Holland, Sweden and Germany. From these studies, it is difficult to clearly demarcate the punitive motive from the therapeutic, and on considering the material reviewed, one is left with the impression that the method of selecting cases for legal castration is far from scientific.

The conclusions arrived at as a result of these studies seem to represent collected opinions rather than validated findings obtained from well-designed statistical analysis.

Dr. Bremer reviews in detail the laws governing castration in Norway and assesses the application of the law in the period before World War II, during the Nazi occupation and in the post-war period. The main body of the book consists of a follow-up study of 216 men and 28 women who were castrated through "due process of the law in Norway between 1935 and 1949".

The reviewer is left with the impression that the author, in his attempt to be objective, tries very hard to find some reasonable medical, legal or social justification for the procedure. Careful analysis of his findings would, however, indicate that this justification is never achieved. The price paid by each individual in contrast to the minimal public gain would lead one to the conclusion that castration offers only a very limited therapeutic advantage. The author sums this up by stating that "to talk about castration as a solution to the problem of sex offenders is absurd." His follow-up study of the 28 women concerned might be summarized by the statement: "The result of legal castration of women seems to be so uncertain and poor, that there is definitely doubt as to its justification." Although one might challenge the design of the author's follow-up experiment, it contains much useful information, especially for those engaged in medical-legal psychiatry.

THE POSTNATAL DEVELOPMENT OF THE HUMAN CEREBRAL CORTEX. LeRoy Conel, Boston University School of Medicine. Vol. VI, The Cortex of the Twenty-four-month Infant. 310 pp. Illust. Harvard University Press, Cambridge, Mass.; S. J. Reginald Saunders and Company Ltd., Toronto, 1959. \$13.75.

This book has been prepared to conform with the previous five volumes of Professor Conel's outstanding monograph.

He uses nine criteria in his assessment of the further development of the cerebral cortex between the age of 15 months (Vol. V, 1955) and 24 months, and he concludes that there is moderate but significant development in these nine months of the infant's life.

In his comments he discusses the recent literature suggesting the role of the cerebrospinal fluid in the transport of these metallic ions to nerve cells, which are necessary for their functional activity. He also describes his observations on the stages in development of Nissl-substance from the nucleoprotein of the nerve cell nucleus.

Like previous volumes, this book is profusely illustrated by plates of each cortical area stained with cresyl violet, Cajal and the Cox-Golgi techniques. Line drawings of the Cox-Golgi sections have been added.

KLINIK UND THERAPIE SYMPTOMATISCHER ANFALLSLEIDEN (Diagnosis and Therapy of Symptomatic Epilepsy). K. Nittner and H. W. Steinmann. EEG UND HIRNTRAUMA (EEG and Brain Injury). H. W. Steinmann. 175 pp. Illust. Georg Thieme Verlag, Stuttgart, 1959. \$8.75.

This is one of a series of monographs on various topics, presented in the light of their importance in the field of social legislation. This series is published under the title "Arbeit und Gesundheit" (Labour and Health) by the German Federal Department of Labour and Social Order for the information of doctors working in the field of social security, with its increasing impact on life in most parts of the world. Accompanied by excellent figures (radiological, angiographic, pneumoencephalographic studies, EEG tracings, and diagrams), these two monographs present valuable experience from the leading German neurosurgical university hospital and research institute under the direction of W. Tönnis. In view of the difficulties still encountered in a great variety of problems regarding the diagnosis, prognosis, and management of brain injuries, these monographs offer a welcome contribution to the study of these problems.

THERAPEUTIC ELECTRICITY AND ULTRAVIOLET RADIATION. Edited by Sidney Licht. 373 pp. Illust. Elizabeth Licht, New Haven, Conn., 1959. \$10.

This book, Vol. 4 of the Physical Medicine Library series, is the work of nine contributors, including Sidney Licht, the editor. It is in two parts, as indicated by the title. The section on therapeutic electricity is distinguished by an excellent and detailed chapter on the history of electrotherapy, contributed by the editor. This is followed by chapters on instrumentation, clinical electrical stimulation, iontophoresis, and electro-sleep therapy. The latter is a contribution of a Russian specialist.

The section on ultraviolet radiation likewise contains an excellent chapter on the historical aspects. This is followed by chapters on instrumentation, physiological effects, and clinical uses of ultraviolet radiation.

This interesting and well-written book can be recommended to students and specialists in the field of physical medicine.

THE MEDICAL SECRETARY. Kenneth B. Coffin and Forest Colwell. 391 pp. Illust. The Macmillan Company, New York; Brett-Macmillan Ltd., Galt, Ont., 1959. \$5.95.

The authors of this comprehensive textbook for medical secretaries gain our good will on their first page when they modestly remark that it is impossible for a textbook of this kind to be completely original, and acknowledge their indebtedness to many sources. They have produced an excellent guide for the secretary in a doctor's office, in a general hospital or in a dentist's office, and have certainly fulfilled their stated intention to provide material for the student now in training for a position in a medical office, the secretary who wishes to become a medical secretary, and the medical assistant whose duties include those of receptionist and secretary. They cover every possible phase of a secretary's office life—dealing with hospital insurance organizations, dealing with patients, filing, book-keeping, and even taking dictation in the operating room. Useful appendices contain a synopsis of the principles of medical ethics, glossaries of common symptoms, common diseases, laboratory tests, eponyms, instruments and abbreviations. There is an appendix on the preparation of manuscripts for dispatch to medical journals. Presentation is good and accurate, and the book will certainly have many friends among those invaluable helpers of the physician.

LOKALANAESTHESIE UND LOKALANAESTHETIKA (Local Anaesthesia and Local Anesthetics). H. Killian. 770 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1959. \$36.65.

Under the editorship of Prof. H. K. Killian, 18 scientists and clinicians from various centres in West Germany, East Germany and Switzerland present a text on local anaesthesia in order to fill the need for a German standard work comparable to Pitkin's *Conduction Anaesthesia* or Bonica's *The Management of Pain*. The result is a respectable book, technically of excellent quality, with over 300 well-reproduced anatomical drawings and photographs.

The text is divided into five principal parts. After a brief historical introduction, almost one-third of the book consists of a discussion of the theoretical back-

ground of local anaesthesia, covering in a scholarly fashion the physiology of pain perception and pain conduction, and the physical and chemical properties of local anaesthetics, as well as their pharmacology and toxicology. Each chapter ends with a rich bibliography, including the important Anglo-American and Russian publications up to 1956-57. A third part is concerned with standard techniques of local anaesthesia, including the various methods of blocking the autonomic nervous system. The next part presents special types of local and conduction anaesthesia in various surgical specialties (ophthalmology, dentistry, otolaryngology, and obstetrics) and also various regions of the body (neck, chest, abdomen and extremities). A chapter on the Russian techniques of local anaesthesia for thoracic surgery is of interest; these consist basically of infiltration anaesthesia and sympathetic blocks, according to the surgical approach. A final part, entitled "Therapeutic Anaesthesia", deals with procaine therapy, which in the last 10 years has aroused enthusiasm in many practitioners in Europe and has frustrated scientists. The phenomenon of sudden disappearance of pain, after intracutaneous injection of procaine into the corresponding dermatomes or after infiltration of an old scar or an infected tooth, has thus far resisted sound scientific explanation, but probably deserves more interest on this continent.

In contrast to the American standard texts cited in the introduction to his volume, the great emphasis on physiology and pharmacology is striking. The theoretical parts include much material but are often written in a review fashion, leaving the reader less firmly grounded in the basic sciences helpless in a confusion of experimental data and references. The clinical chapters often lack an opinion based on practical experience as guidance for the student in this field. Instead of presenting definite principles of management, the authors occasionally take refuge in theoretical generalities presented in a language difficult to understand for one not thoroughly familiar with the "medical climate" in Germany at the time this book was written. This is particularly noticeable in regard to the role played by chlorpromazine and the "cocktails" (also referred to as "ganglion blockers"), and by the theories to which they gave rise. Keeping this in mind, a statement in reference to epidural anaesthesia like "premedication with promethazine and chlorpromazine is far superior to the prophylactic use of peripherally acting drugs for the support of the circulation" does have a less shocking effect; the addition of 1-2 mg. (!) of noradrenaline to the anaesthetic solution for epidural anaesthesia, recommended in an adjoining sentence, may be helpful in such a regimen. In general, vasopressors with the exception of noradrenaline are considered either of little value or harmful in spinal anaesthesia and are not discussed further. In contrast to American books, there is hardly any reference to the use of alcohol and similar agents for therapeutic blocks.

The mostly schematic anatomical illustrations are well chosen, but they do not always convey the essentials of a technique without reference to the text. This limits the use of this book to those familiar with the German language, who will find it a very valuable addition to their library and a most useful reference work on all aspects of local anaesthesia.

(Continued on page 874)



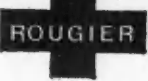
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(Continued from page 872)

IMMUNOPATHOLOGIE (Immunopathology). 1ST INTERNATIONAL SYMPOSIUM. Edited by Pierre Grabar, Paris, and Peter Miescher, Basel. 520 pp. Illust. Benno Schwarz & Co., Basel/Stuttgart; Intercontinental Medical Book Corporation, New York, 1959. \$16.25.

Since the advent of the concept of auto-immunity, immunologists and pathologists have become aware of a need for close co-operation. Serological investigations are no longer sufficient in the assessment and explanation of disease processes with an allergic etiology. The morphological stigmata of immunological tissue injury are still incompletely defined.

This book represents the first fruits of the correlated and integrated work of these two specialties on a world-wide scale. Experimental immunopathological papers are grouped side by side with clinico-pathological reports. For example, studies on experimental Masugi-type nephritis are followed by a study on the role of auto-antibodies in human glomerulo-nephritis; a paper on experimental aspermatogenesis is followed by an account of auto-antibodies against spermatozoa in sterile men, and a discussion of experimental immunological thyroiditis is followed by considerations of auto-immune thyroiditis in men. Other subjects discussed include the properdin system, agammaglobulinæmia, organ-specific immunopathology, rheumatoid arthritis and systemic lupus. The immunologist's contribution is reflected in the application of newer procedures, such as the tanned red cell agglutination test, the agar-gel diffusion technique, and the study of behaviour of isotope-labelled antigens. The pathologist's efforts are

shown in the use of fluorescent and electron microscopy.

Despite the aim of the editors to make this book "a baseline for clinical exploitation of experimental immunopathology", the symposium remains essentially a tool in the hands of the experimental pathologist and immunologist. The papers on rheumatoid arthritis and systemic lupus erythematosus are perhaps the exception.

In its 520 pages of trilingual text (German, English and French), many problems are touched upon but few are answered. The value to the English-speaking reader lies in its bringing together material so far available only in one German textbook (Miescher, P. and Vorlaender, K. O.: *Immunopathologie in Klinik und Forschung*, Georg Thieme Verlag, Stuttgart, 1957).

The book is an excellent review of present concepts in immunopathology and serves to point to the gaps existing in our knowledge of even the basic processes involved in cellular injury resulting from antigen-antibody interaction.

UEBER DIE ERBLICHKEIT DES NORMALEN ELEKTROENCEPHALOGRAMMS. Vergleichende Untersuchungen an ein- und zweieiigen Zwillingen (Inheritance of the Normal Electroencephalogram. Comparative Investigations in Uniovular and Binovular Twins). E. Vogel, Berlin. 92 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1958. \$2.30.

In his introduction to this little book Professor Nachtsheim remarks sourly that although twin studies are now all the rage, their findings are often limited to a demonstration that uniovular twins resemble each other more closely than binovular. He then hastens to add that the present monograph goes much further than such a demonstration. Vogel bases his studies on 208 pairs of twins, 110 uniovular and 98 binovular, aged from 6 to 13 years, whose electroencephalograms (EEG) he studied with a 16-channel recorder with eight leads simultaneously recorded from each twin. Whereas basal rhythm was the same in both of a pair of uniovular twins, it was dissimilar in two-thirds of binovular twins. Vogel discusses the different details of the EEG, with particular emphasis on those in which a difference was detected between the members of a uniovular twin pair. He stresses the need in twin studies for demonstrating such differences, and finding out whether they are constant and reproducible over a prolonged period, and finally analyzing their origins.

METHODS FOR RESEARCH IN HUMAN GROWTH. Stanley M. Garn, Fels Research Institute, Yellow Springs, Ohio, and Zvi Shamir, Hadassah-Hebrew University Hospital and Medical School, Jerusalem, Israel. 121 pp. Illust. Charles C Thomas, Springfield, Ill.; The Ryerson Press, Toronto, 1958. \$5.25

Despite its small size, this book should prove of real value to those very large numbers of medical personnel concerned with normal and abnormal development of the growing child.

The various methods are presented in an admirably clear fashion, the aims and pitfalls of such research being equally emphasized. Problems of planning, selection, maintenance of records and interpretation of data are adequately covered. The language is simple and terse and should appeal to the very busiest worker in the field.

(Continued on page 879)

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ACETYLSALICYLIC ACID	0.23 Gm.
PHENACETIN	0.16 Gm.
CAFFEINE	0.03 Gm.



CORICIDIN

FORTE CAPSULES

analgesic
antipyretic
antiallergic
decongestive
supportive
restorative

fortified relief for the severe cold

The clinically proved Coricidin formula (with antihistamine in full therapeutic dosage) plus methamphetamine to counteract depression and fatigue and Vitamin C for stress support.

DOSAGE: One Capsule every four to six hours.

EACH RED AND YELLOW CAPSULE CONTAINS:

CHLOR-TRIPOLON MALEATE	4 mg.
(chlorprophenpyridamine maleate)	
ACETYLSALICYLIC ACID	190 mg.
PHENACETIN	130 mg.
CAFFEINE	30 mg.
ASCORBIC ACID	50 mg.
METHAMPHETAMINE HYDROCHLORIDE	1.25 mg.

On Rx and cannot be refilled without your permission.

CORICIDIN for complicated colds

for colds accompanied by aches and pains

CORICIDIN with PENICILLIN TABLETS

analgesic
antipyretic
antibiotic
antihistaminic

to prevent complications due to colds

The usual adult dosage is 4 to 6 tablets daily, taken one hour before or two hours after meals. Treatment should be instituted promptly upon appearance of upper respiratory infection and should be continued for 24 to 48 hours after temperature is normal.

EACH CORICIDIN WITH PENICILLIN TABLET CONTAINS:

PENICILLIN G PROCAINE.....	150,000 units
CHLOR-TRIPOLON MALEATE.....	2 mg.
(chlorprophenpyridamine maleate)	
ACETYLSALICYLIC ACID.....	0.15 Gm.
PHENACETIN.....	0.12 Gm.
CAFFEINE.....	0.03 Gm.

CORICIDIN with CODEINE TABLETS (1/4 or 1/8 gr.)

analgesic
sedative
antipyretic
antihistaminic

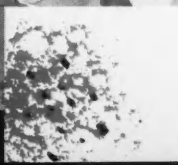
when pain is a dominating factor

Added sedative-analgesic action of codeine provides more effective relief in grippal conditions and other pain disorders.

DOSAGE: One tablet, containing either 1/8 or 1/4 grain of codeine, every four to six hours.

EACH CORICIDIN WITH CODEINE TABLET CONTAINS:

CODEINE PHOSPHATE..	8 mg. or 0.016 Gm. (1/8 or 1/4 gr.)
CHLOR-TRIPOLON MALEATE.....	2.0 mg.
(chlorprophenpyridamine maleate)	
ACETYLSALICYLIC ACID.....	0.23 Gm.
PHENACETIN.....	0.15 Gm.
CAFFEINE.....	0.03 Gm.





CORICIDIN

in pediatric practice



CORICIDIN

PEDIATRIC MEDILETS

(no caffeine)

analgesic
antipyretic
antihistaminic

children's sneezes, sniffles, fever

...respond to these cherry-flavoured, color-flecked tablets.

DOSAGE: Under six years: one-quarter to one Medilet.

Six to twelve years: one to two Medilets.

Each dose may be repeated every three to four hours for up to three days.

EACH CORICIDIN PEDIATRIC MEDILET CONTAINS:

CHLOR-TRIPOLON MALEATE 0.75 mg.

(chlorprophenpyridamine maleate)

ACETYLSALICYLIC ACID 80 mg.

PHENACETIN 16 mg.



CORICIDIN

PEDIATRIC DROPS

analgesic
antipyretic
antihistaminic

when youngsters protest the cold

...or discomforts of inoculations, teething, allergies, prickly heat.

DOSAGE: (Based on every four hours as required.)

Over five years, 1.5 cc.

Two to four years, 1 cc.

Under two years, 0.5 cc. to 1 cc.

PACKAGING: 15 cc. bottles with calibrated plastic dropper

COMPOSITION: Per cc.

CHLOR-TRIPOLON MALEATE 2 mg.

(chlorprophenpyridamine maleate)

SODIUM SALICYLATE 100 mg.

AMINOACETIC ACID 50 mg.

(In an aqueous raspberry flavoured solution)



CORICIDIN

SYRUP

antitussive
analgesic
antihistaminic

**for the coughing patient
of any age**

DOSAGE: Adults, one teaspoonful initially, followed by another in one hour. Thereafter, one teaspoonful three to four times daily. Children six to twelve years, one-half adult dosage.

Younger Children: Adjust dosage according to age.

PACKAGING: Bottles of 3 oz. and 16 oz.

EACH 5 cc. TEASPOONFUL OF CORICIDIN SYRUP CONTAINS:

CHLOR-TRIPOLON MALEATE 2 mg.

(chlorprophenpyridamine maleate)

DIHYDROCODEINONE BITARTRATE 1.67 mg.

SODIUM SALICYLATE 225 mg.

CAFFEINE 30 mg.

GLYCERYL GUAIACOLATE 30 mg.

SODIUM CITRATE 120 mg.

Schering
CORPORATION LIMITED



MONTREAL

(Continued from page 874)

MEDICAL HISTORY OF THE SECOND WORLD WAR. ARMY MEDICAL SERVICES, CAMPAIGNS. Vol. III. F. A. E. Crew. 645 pp. Illust. Her Majesty's Stationery Office, London, 1959. £5.

This is the third volume on campaigns of the United Kingdom Army Medical Services during the Second World War. It records the story of military medicine, and of the men who practised it in the campaigns which began with the invasion of Sicily in July 1943, followed by the invasion of Italy in September of that year. The campaign in Italy throughout 1944 to its ending in May 1945 is skilfully recorded. The final chapter is devoted to the medical history of the return to Greece which began in October 1944.

It has been said that the campaigns in Sicily and Italy in 1944-45 were among the most brilliant and successful fought in the Second World War. There were no hurried and disorderly retreats and no lightning and long advances. All actions took place in a crowded country with a teeming population with a distinctly low level of living. The social and economic life of the country had been profoundly disturbed by war. Malaria, dysentery, typhoid and venereal disease were widespread, and typhus at times assumed epidemic proportions. The Allied Armies that fought these campaigns were made up of a great variety of national groups, with widely differing social organizations. They were called upon to endure the intense cold of winter in the mountains and the sweltering heat of summer in the plains. The physical environment was as harsh as any environment could be. Frequently military strength and efficiency were more gravely threatened by disease than by injuries due to the enemy, whose defence tactics throughout the campaigns were skilful, stubborn and determined. There were many stubbornly contested battles resulting in large numbers of casualties. The military situation, the terrain and the weather frequently combined to impede evacuation and on occasion temporarily made it impossible. The work of the medical services furthermore was by no means restricted to maintenance of health among troops and treatment of battle casualties. At times it was even more important to safeguard the health of civilians, ravaged by disease and often destitute and half-starved. All this was accomplished with great success as evidenced by a statement in the preface of this volume, "Never before, either in war or peace, had everything that medicine had to contribute to the promotion of health, to the prevention of disease and to the treatment of disease and of injury, been as easily and as readily available to the individual member of a community as was the case in Italy (and other theatres of war not too dissimilar thereto)."

This outstanding narrative will be of particular interest to Canadians as it includes the complete story of the outstanding contributions made by our Services—the fighting troops as well as the Army Medical Services.

SKIN DISEASES IN THE AFRICAN. G. H. V. Clarke. 172 pp. Illust. H. K. Lewis & Co. Ltd., London, 1959. £4. 4s.

Since the atlas by E. C. Smith published in 1932 has become unobtainable, the present work is apparently the only one devoted to dermatology in the Negro. Photography is in black and white and there is a minimum of explanatory text to accompany

**T
R**
IMPORTANT
TO YOU? Upjohn
SEE PAGE 88

the pictures. The conditions illustrated represent skin diseases common to both Africans and Europeans, skin diseases common in Africans but uncommon in Europeans and vice versa, and skin diseases rare in both races. An introductory chapter discusses the physiology and histology of the skin in the African, and concluding chapters deal with fungous diseases and venereal diseases. There is an excellent bibliography and an adequate index.

DER BIOLOGISCH-ANTHROPOLOGISCHE (EXISTENTIELLE) AUFBAU DER PERSÖNLICHKEIT (The Biological and Anthropological (Existential) Structure of Personality). G. Ewald. 67 pp. Illust. Georg Thieme Verlag, Stuttgart; Intercontinental Medical Book Corporation, New York, 1959. \$2.35.

This is an attempt to present man in his "total existence", including the specific human anthropological view. This attempt is based on Nicolai Hartmann's "ontology" and embraces all levels of "being": the lowest, material being (chemical-physical level with its scientific laws of causality); the next higher or "organismic" being (showing the preservation of the individual and of the species, rhythms of life, and the lowest instinctual drives); the higher, psychic being with its emotions and affects; finally, the highest level of spiritual being owned only by man. In his efforts to form his individual personality from the resources of his psychic sphere, man is restricted by space and time because of his bodily ties and his functions. Therefore he needs metaphysical relations which are felt to be of great importance regardless of whether they are called religion or a "philosophical creed" in the divine spark of "reason".

MEDICAL FILMS

CONTINUING the listing of available films on medical and related subjects, we list below additional films. The films are held in the National Medical and Biological Film Library and are distributed by the Canadian Film Institute, 142 Sparks Street, Ottawa, Ontario. The evaluations have been prepared by Canadian specialists in the subjects of the films, under the Medical Committee of the Scientific Division of the Canadian Film Institute, which is headed by Dr. G. H. Ettinger.

SURGERY

Acute Appendicitis—1939; Silent; B & W; 32 minutes.

Produced by Eastman Medical Films (now Encyclopædia Britannica Films Inc.). Technical Adviser: Edward Martin, M.D., Philadelphia, Pa.

Description.—Illustrates the pathology and diagnosis of acute appendicitis, and the technique of appendectomy. The film is in two parts, mounted on separate reels. Part I deals with anatomy, pathology and diagnosis. Part II illustrates and describes (live photography) an appendectomy.

Appraisal (1945).—This is a very well conceived instructional film, despite its age. Development of the subject through anatomy, pathology and surgical treatment is very well done and the basic principles shown are still true; up-to-date with exception of chemotherapy and non-use of Miller-Abbott tube. Considered an excellent film for medical students. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$3.00). Purchase (in Canada) from General Films Limited, 1534-13th Avenue, Regina, Sask.

Anterior and Posterior Plaster Beds—1937; Silent; B & W; 11 minutes.

Produced by the Abergale Sanatorium, Manchester, England.

Description.—An instructional film, illustrating a technique of application of plaster-of-Paris splints. Anterior plaster beds are shown as used in the treatment of tuberculous disease of the spine when radiological evidence demonstrates commencing recalcification and approximation of affected vertebral bodies. Posterior plaster beds are shown as used in the treatment of tuberculous disease of the low and mid dorsal spine. In both cases the film gives a step-by-step demonstration of the application of plaster.

Appraisal (1945).—In this rather old film the principles demonstrated are sound and the plaster work is excellent; it is recommended for medical students, interns, nurses, general practitioners and orthopaedic specialists. Animation has been used to good advantage; subtitles are good; black-and-white photography is only fair. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$1.00). No longer available for purchase.

An Aseptic Method of Uretero-Intestinal Anastomosis with Divisible Carrier—1939; Silent; Colour; 36 minutes.

Produced by Frank Hinman, M.D., University of California Hospital, San Francisco, California.

Description.—A record-instructional film, illustrating the surgical operation described in the film title.

Appraisal (1945).—A very well planned film in which a very detailed operative procedure has been made clear by the use of diagrammatical drawings to demonstrate first the procedures to be carried out. This is a special operative technique, not in common use; the author is a leading authority and the technique may come into greater use; basic principles are up-to-date. The film is of interest to surgeons rather than to medical students; it is therefore recommended for surgeons and it is suitable for senior medical students, interns and other medical groups. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$5.00). For purchase apply to Frank Hinman, M.D., University of California Hospital, San Francisco, California.

Carcinoma of the Left Breast: Radical Mastectomy (Transverse Incision)—1940; Silent; Colour; 17 minutes.

Produced by S. W. Harrington, M.D., Mayo Clinic, Rochester, Minnesota.

Description.—A record-instructional film, illustrating the surgical treatment of carcinoma of the left breast, using the transverse incision.

Appraisal (1945).—An excellent film, recommended for specialists in surgery and suitable for senior medical students, interns and general practitioners. As it deals mainly with operative technique and only very briefly with diagnosis, the film is more suitable for surgeons than for medical students. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$2.00). For purchase apply to the Section on Photography, Mayo Clinic, Rochester, Minnesota.

Cataract Extraction—1944; Silent; Colour; 26 minutes.

Produced by J. S. Guyton, M.D., Wilmer Institute, Johns Hopkins Hospital, Baltimore, Maryland.

Description.—This record-instructional film illustrates the procedures, in sequence, of intracapsular cataract extraction.

Appraisal (1945).—All details are well shown, with repetition of several of the steps so that no manoeuvres can be missed. This film is up-to-date and is recommended for students and specialists in ophthalmology; also suitable for senior medical students and other interested medical groups. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$4.00). For purchase apply to Dr. J. S. Guyton, Assistant Director, Wilmer Institute, Johns Hopkins Hospital, Baltimore 5, Maryland.

Defibrillation of the Heart—1949; Silent; Colour; 15 minutes.

Produced by Claude S. Beck, M.D., Revascularization of the Heart Research Laboratory, Western Reserve University, Cleveland, Ohio.

Description.—A record-instructional film, demonstrating ventricular fibrillation and its therapy.

Appraisal (1950).—While this film is not a finished cinematographic production and suffers from lack of any introduction to the subject, the sequences showing ventricular fibrillation in animal hearts are excellent and the demonstration of various possible therapeutic procedures is quite effective. Despite its shortcomings, this film is recommended for thoracic surgeons, medical students in the clinical years and for those interested in cardiac physiology. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$2.00). For purchase apply to Claude S. Beck, M.D., Lakeside Hospital, 2065 Adelbert Road, Cleveland 6, Ohio.

Endoscopic Electrosection of the Prostate—1937; Silent; Colour; 11 minutes.

Produced by Roger W. Barnes, M.D., Department of Surgery, College of Medical Evangelists, Los Angeles, California.

Description.—An instructional-record film, illustrating the apparatus and a procedure for endoscopic electrosection of the prostate.

Appraisal (1945).—The film is recommended for senior medical students, interns and surgeons. It is a clearly presented and well-developed portrayal of a standard up-to-date procedure. The special effect using the anatomical specimen is extremely good. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$2.00). For purchase apply to Roger W. Barnes, M.D., 1216 Wilshire Boulevard, Los Angeles, 14, California.

Fillet and Spica Plaster—1937; Silent; B & W; 16 minutes.

Produced at the Abergale Sanatorium, Manchester, England.

Description.—An instructional film, illustrating a technique of applying plaster-of-Paris splints.

Appraisal (1945).—A good film, although the black-and-white photography is mediocre. The principles are still

basically sound and the plaster work is very good. There is considerable emphasis on the use of one particular commercial type of plaster. Animation has been used to advantage. The film is recommended for medical students in the clinical years, interns, nurses, general practitioners and orthopaedic specialists. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$1.00). No longer available for purchase.

Genito-Urinary Surgery for the General Practitioner—1938; Silent, Colour; 26 minutes.

Produced by Roger W. Barnes, M.D., Department of Surgery, College of Medical Evangelists, Los Angeles, California.

Description.—An illustration of surgical techniques for (1) suprapubic cystotomy, (2) circumcision in the adult, (3) hydrocelectomy, and (4) repair of a ruptured bladder.

Appraisal 1946.—An instructional-record film, recommended for general surgeons and interns. The film is well done and the procedures shown would be very instructive to the general surgeon, although too technical for undergraduate medical students. The subject matter is clearly presented, animation is used to good advantage, explanatory subtitles are good and the techniques shown are up-to-date. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$4.00). For purchase apply to Roger W. Barnes, M.D., 1216 Wilshire Boulevard, Los Angeles, California.

Hypodermic Syringes and Needles: Their Care and Function—1943; Sound; Colour; 35 minutes.

Produced by Mervin W. LaRue, Chicago, for Becton, Dickinson & Company. Technical Advisers: An advisory committee of operating room supervisors and nurses, appointed by the American College of Surgeons.

Description.—This instructional-training film shows the manufacture and care of syringes and needles and demonstrates techniques of injection.

Appraisal (1945).—An up-to-date and clearly presented film, of value and recommended as a teaching aid for student nurses. Suitable for other interested medical and nursing groups and scientific audiences. Inappropriate for non-scientific audiences.

Availability.—National Medical and Biological Film Library (\$4.50). For purchase apply to Becton, Dickinson & Company, Rutherford, N.J.

Indirect Inguinal Hernia—1929; Silent; B & W; 42 minutes.

Produced by Eastman Medical Films (now Encyclopædia Britannica Films Inc.). Technical Adviser: Daniel LeRay Borden, M.D., Washington, D.C.

Description.—An instructional film, illustrating the anatomical and clinical aspects of indirect inguinal hernia, and the essential steps in its surgical repair.

Appraisal (1946).—Despite its age this is an excellent teaching film for senior medical students and interns; also suitable for practising surgeons. Animation has been used to great advantage; subject matter is clearly presented and well developed. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$4.50). Purchase (in Canada) from General Films Limited, 1534 - 13th Avenue, Regina, Sask.

Nephropexy—1939; Silent; Colour; 29 minutes.

Produced by Elmer Belt, M.D., Los Angeles, California. *Description.*—An instructional-record film, demonstrating a surgical technique for right nephropexy.

Appraisal (1945).—The film is well conceived and carried out; the anatomical part is very well done and the operative approach is very clear. While nephropexy is not in as high favour as some years ago, the technique shown is a good one and the film is recommended for surgeons, as well as being suitable for senior medical students and other interested medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$4.00). For purchase apply to Elmer Belt, M.D., 1893 Wilshire Blvd., Los Angeles 5, California.

New Limbs for Old—1945; Sound; Colour; Part I: 45 minutes, Part II: 13 minutes.

Produced by the Combined Orthopaedic Unit, Christie Street Hospital, Department of Veterans Affairs, Toronto, Ontario, with the co-operation of the National Film Board of Canada.

Description.—An instructional-training film, demonstrating types of amputations and prostheses.

Appraisal (1950).—A good film, with good techniques, although the prostheses are somewhat dated. Recommended for orthopaedic specialists and for limb-makers and similar technicians, and useful for persons or groups interested in rehabilitation or dealing with amputees. Inappropriate for most non-medical audiences.

Availability.—National Medical and Biological Film Library (Part I—\$5.00) (Part II—\$2.25). Purchase from Distribution Branch, National Film Board of Canada, P.O. Box 6100, Montreal 3, Quebec.

Operative Treatment of Lung Abscess: All Stages—1940; Silent; Colour; 17 minutes.

Produced by the Thoracic Surgery Department, University of California Medical School.

Description.—A record-instructional film, showing a one-stage and a multiple-stage surgical procedure for the treatment of lung abscess.

Appraisal (1945).—Operative procedure is well developed, but the indications for the procedure are not. Emphasis on the multiple-stage operation is not in keeping with modern trends. Film, however, warrants inclusion in Library and is recommended for surgeons. Also suitable for senior medical students and other medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$2.00). For purchase apply to Thoracic Surgery Department, University of California Medical School, San Francisco 22, California.

Orchiopexy—1940; Silent; Colour; 16 minutes.

Produced by James C. Sargent, M.D., Milwaukee, Wisconsin.

Description.—A record-instructional film, illustrating a technique of replacement of the cryptorchid testicle.

Appraisal (1945).—The film is recommended for surgeons. The technique is up-to-date and, although there are a variety of procedures for this condition, this one is quite popular. No mention is made of hormonal therapy. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$2.00). For purchase apply to James C. Sargent, M.D., 324 East Wisconsin Avenue, Milwaukee 2, Wisconsin.

Perineo-Abdominal Excision of the Rectum in One Stage—1934; Silent; B & W; 17 minutes.

Produced by W. B. Gabriel, M.D., M.S., F.R.C.S., London, England.

Description.—A record-instructional film, illustrating a one-stage operation for the abdomino-perineal excision of the rectum.

Appraisal (1945).—The film is only fair: the photography cannot compare with today's colour films, and the film deals with a very complicated operative procedure which has never been generally popular. It may, however, be of interest to senior medical students and surgeons. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$1.00). No longer available for purchase.

Segmental Resection of a Portion of the Stomach and Gastroenterostomy for Certain Benign Gastric Ulcers—1940; Silent; Colour; 22 minutes.

Produced by Waltman Walters, M.D., Division of Surgery, Mayo Clinic, Rochester, Minnesota.

Description.—A record-instructional film, illustrating a surgical technique for segmental resection of a portion of the stomach and gastroenterostomy for certain benign gastric ulcers.

Appraisal (1945).—The operative technique is very clearly and well presented, and the film is recommended for

specialists in this type of surgery. While this technique, recommended by the Mayo Clinic, has not been generally accepted, the film nevertheless warrants inclusion in the Library. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$3.00). For purchase apply to Section on Photography, Mayo Clinic, Rochester, Minnesota.

Studies of Battle Casualties—1946; Sound; Colour; 27 minutes.

Produced by the National Film Board of Canada, for the Department of National Defence, from film photographed by Lieut-Col. A. L. Chute, R.C.A.M.C., in Italy in 1944.

Description.—An instructional film, illustrating bodily reaction to and surgical closure of war wounds.

Appraisal (1946).—An excellent film, with photography surprisingly good for the conditions under which it was done. Cases are typical. The film is recommended for senior medical students, interns, surgeons, and all interested medical audiences. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$4.50). For purchase apply to the Distribution Branch, National Film Board of Canada, P.O. Box 6100, Montreal 3, Quebec.

Surgical Approaches to the Ankle Joint—1952; Sound; Colour; 32 minutes.

Produced by Department of Medicine and Surgery, U.S. Veterans Administration. Surgery and medical supervision by Leroy C. Abbott, M.D., et al., University of California Medical School.

Description.—An instructional-training film, demonstrating the surgical anatomy and some surgical approaches to the ankle joint.

Appraisal (1952).—An effective film. As are the other films in the "Surgical Approaches" series, this is a splendid usage of the motion picture to teach applied anatomy and the surgery based upon it. Recommended for orthopaedic surgeons and medical students in the clinical years; suitable for other interested medical groups, such as operating-room nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$6.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

Surgical Approaches to the Elbow Joint—1950; Sound; Colour; 38 minutes.

Produced by Department of Medicine and Surgery, U.S. Veterans Administration. Surgery and medical supervision by Leroy C. Abbott, M.D., et al., University of California Medical School.

Description.—An instructional-training film, illustrating the anatomy of and the surgical approaches to the elbow joint.

Appraisal (1951).—An excellent and very well done film, in the "Surgical Approaches" series. Recommended for orthopaedic surgeons and medical students in the clinical years; suitable for other interested medical groups, such as operating-room nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$7.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

Surgical Approaches to the Hip Joint—1951; Sound; Colour; 36 minutes.

Produced by Department of Medicine and Surgery, U.S. Veterans Administration. Surgery and medical supervision by Leroy C. Abbott, M.D., et al., University of California Medical School.

Description.—An instructional-training film, demonstrating the anatomy of the hip joint and some suitable surgical approaches.

Appraisal (1952).—An excellent film, in the "Surgical Approaches" series, with anatomy extremely well illustrated, and demonstrating standard approaches. Recommended for orthopaedic surgeons and medical students in the clinical years; suitable for other interested medical audiences, such as operating-room nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$7.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

Surgical Approaches to the Joints of the Foot—1951; Sound; Colour; 32 minutes.

Produced by Department of Medicine and Surgery, U.S. Veterans Administration. Surgery and medical supervision by Leroy C. Abbott, M.D., et al., University of California Medical School.

Description.—An instructional-training film, demonstrating the anatomy of the foot and some suitable surgical approaches to the joints of the foot.

Appraisal (1952).—An excellent film. Anatomy is extremely well illustrated and is more adequate than the surgical technique; we doubt the advisability of illustrating wire fixation through the stem of the foot in a teaching film. Recommended for orthopaedic surgeons and medical students in the clinical years; suitable for other interested medical audiences, such as operating-room nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$6.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

Surgical Approaches to the Joints of the Wrist—1952; Sound; Colour; 33 minutes.

Produced by Department of Medicine and Surgery, U.S. Veterans Administration. Surgery and medical supervision by Leroy C. Abbott, M.D., et al., University of California Medical School.

Description.—An instructional-training film, demonstrating the surgical anatomy and showing some approaches to the joints of the wrist.

Appraisal (1952).—An effective film, with anatomy extremely well illustrated and techniques acceptable. As are the other films in this "Surgical Approaches" series, this is a splendid usage of the motion picture to teach applied anatomy and the surgery based upon it. Recommended for orthopaedic surgeons and medical students in the clinical years; suitable for other interested medical audiences, such as operating-room nurses. *Unsuitable for non-medical audiences.*

Availability.—National Medical and Biological Film Library (\$6.00). Purchase from United World Films Inc., 1445 Park Avenue, New York 29, N.Y.

(To be continued)

The Shute Parallel Forceps: Its Techniques and Clinical Use—1959; Sound; Colour; 30 minutes.

Produced by Mars Film Productions Limited—Producer and Director, Emil O. MacQuat. Clinical sequences filmed at the Ottawa Civic Hospital, Ottawa, Canada. Introduction, manikin illustrations, clinical demonstrations, with commentary and final summary by Wallace B. Shute, M.R.C.O.G., F.R.C.S.[C].

Description.—A film comprising the following features: (1) Introduction—discussing briefly the history of obstetrical forceps in general and the development of the parallel forceps in particular. (2) A comparison between the five types of forceps in major use today and the parallel forceps showing the special features of the latter. (3) Comparison between the fitting of the scissors and parallel forceps to a fetal head. (4) Then follow in order—clinical demonstration of occiput anterior, simple occiput transverse, occiput transverse with asynclitic head, forceps on the after-coming head, occiput posterior positions. Each of these is preceded by a manikin demonstration showing the exact manoeuvres used in each type of delivery. (5) Demonstration of a new method of episiotomy suture which gives painless wound after two days. (6) Summary of the advantages of the parallel forceps.

Availability.—The Professional Services Department, Webber Pharmaceuticals Limited, 393 Weston Road, Toronto, Ontario, Canada.

CHILDREN'S AID SOCIETY OF METROPOLITAN TORONTO requires director of medical services. Responsibility involves the direction of clinical services for children from infancy to sixteen years of age in a central and two branch offices. Included in the services are dental and psychiatric clinics. Qualifications: license to practise in Ontario and certification in paediatrics by the Royal College of Physicians and Surgeons of Canada, or its equivalent. Apply in writing to the Executive Director, Children's Aid Society of Metropolitan Toronto, 33 Charles Street E., Toronto 5, Ont.

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NOTE: To avoid the publication of misleading information, all advertisers under the classification "Practices" in the Canadian Medical Association Journal should furnish the following information:

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HOUSE AND PRACTICE FOR SALE in a Central Ontario town. Records, office equipment and introductions included. Owner wishing to specialize. Reply to Box 510, CMA Journal, 150 St. George St., Toronto 5, Ont.

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Residencies and Internships

ST. LUKE HOSPITAL, in Montreal, capacity 451 beds, is considering applications for internship or residency in the different services of a general hospital. The institution is approved with full accreditation by the Joint Commission on Accreditation of Hospitals. The Royal College of Physicians and Surgeons of Canada approves for advanced graduate training the following specialties: anaesthesia, general surgery, internal medicine, orthopaedic surgery, otolaryngology, pathology, radiology (diagnostic) and radiology (therapeutic). Applicants may address their applications to Dr. H. I. Tetreault, Medical Superintendent.

WANTED.—ASSISTANT RESIDENT IN ANAESTHESIA at Sunnybrook Hospital for one year beginning January 1, 1960. Salary \$3000 per annum. Also senior intern in anaesthesia immediately for one year. Salary \$2100. Please address all letters of inquiry to Chief Anaesthetist, Sunnybrook Hospital, Toronto 12, Ontario.

CHIEF RESIDENT AND ASSISTANT RESIDENT IN PAEDIATRICS required by Canadian Teaching Hospital. Regina General Hospital is University approved, has 806 beds of which 236 are paediatric. Active undergraduate and postgraduate teaching program approved for credit towards specialty certification. Stipend at the rate of \$250 and \$200 per month, plus full maintenance. Apply to Dr. A. C. Pickles, Medical Director, Regina General Hospital, Regina, Saskatchewan.

PSYCHIATRIC RESIDENCE.—HOSPITAL WITH LARGE MEDICAL STAFF OFFERS FULLY-ACCREDITED THREE-YEAR TRAINING PROGRAM BEGINNING JULY 1, 1960 FOR MEN AND WOMEN GRADUATES OF CANADIAN OR AMERICAN MEDICAL SCHOOLS DESIRING CERTIFICATION IN PSYCHIATRY. INCLUDES POSTGRADUATE COURSE, GUEST LECTURES, TRAINING IN MODERN THERAPEUTIC PROCEDURES AND SUPERVISED WORK IN MENTAL HYGIENE CLINICS. LIBERAL SALARY INCLUDES FAMILY MAINTENANCE. REPLY TO BOX 469, CMA JOURNAL, 150 ST. GEORGE ST., TORONTO 5, ONT.

ANAESTHESIA RESIDENCIES.—APPLICATIONS INVITED for one or two-year periods beginning January 1 and July 1, 1960. Approved by Royal College of Canada for two years' training towards certification in anaesthesia. This 700-bed teaching hospital has an organized staff and the training program is integrated with the University of Alberta. Apply: Associate Superintendent, Royal Alexandra Hospital, Edmonton, Alberta.

AVAILABLE JULY 1, 1960.—Approved internships (rotating) and residencies in medicine and obstetrics-gynaecology; surgical residencies approved for training in preparation for surgical specialties; 310-bed general hospital, modern, well-equipped; resident training programme; house staff allowed full range under proper medical supervision; full maintenance and uniforms; monthly stipend—interns \$200, assistant residents \$250, senior residents \$300. E.C.F.M.G. certification necessary for foreign graduates. Lawrence and Memorial Hospitals, New London, Connecticut, Hilliard Spitz, M.D., Chairman, Committee on Interns and Residents.

RESIDENCIES IN ANAESTHESIA.—The University of Toronto and affiliated teaching hospitals, offer a three year course in preparation for certification and Fellowship in the Royal College of Physicians and Surgeons of Canada. Enrollment dates are the first of January, April and July, 1960. Address enquiries to, Dr. S. M. Campbell, Associate Professor and Head of the Department of Anaesthesia, University of Toronto.

THE OTTAWA CIVIC HOSPITAL, OTTAWA, ONTARIO invites applications for resident, assistant resident and junior rotating interns for the 1960-61 term. This is a teaching hospital of 962 beds including 90 bassinets, fully-accredited by the Canadian Council on Accreditation and is affiliated with the University of Ottawa Medical Faculty. All inquiries should be addressed to the Assistant Superintendent.

GENERAL PRACTICE RESIDENCY.—Fully-accredited by J.C.A.H. Staffed by clinic group closely associated with hospital. Only graduates of approved medical schools or E.C.F.M.G. certified will be considered. Salary \$6000 yearly. Positions available January 1, 1960 and July 1, 1960. Contact: Director, The Lynn Hospital, Detroit, Michigan.

INTERNS REQUIRED for 400 bed modern, well-equipped, active General Hospital located in Oshawa, Ontario, Canada, an industrial city of 50,000, thirty miles east of Toronto. Remuneration for British graduates \$250 per month. For further particulars, please write Superintendent, Oshawa General Hospital.

WESTMINSTER HOSPITAL has the following positions available from July 1, 1960 to June 30, 1961: Assistant residencies in anaesthesia, radiology, medicine, psychiatry and surgery at \$250 per month. Senior internships in medicine and surgery at \$225 per month. Westminster Hospital is conducted by the Department of Veterans Affairs, and is a 1500-bed hospital with both general treatment and psychiatric divisions. It is approved for training by the Royal College of Physicians and Surgeons of Canada, and is closely integrated into the teaching program of the University of Western Ontario Medical School. For further particulars apply to Chairman of the Intern Committee, Westminster Hospital, London, Ontario.

WESTERN CANADA—ROTATING INTERNSHIPS FOR 1960-61. 350-bed general hospital, fully-accredited, university medical school affiliation; 9700 admissions, 1200 births, 12,200 out-patient visits; very active teaching programme; monthly stipend \$225 and assistance with transportation to Saskatchewan. For further particulars apply to the General Superintendent, Saskatoon City Hospital, Queen Street and 7th Avenue, Saskatoon, Sask.



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MEDICAL NEWS in brief

(Continued from page 846)

SERUM HYPERTONICITY SECONDARY TO CEREBRAL DISEASE

An opportunity occurred to perform balance studies on a patient during recovery from severe serum hyperosmolarity secondary to purulent meningitis. During this recuperative phase, no salt was taken in the diet, serial measurements of electrolyte solutes in the plasma were carried out, and the total volume of urine was collected and analysed for concentration of solutes. The phase of return to normal osmolarity of the serum was characterized by (1) a markedly positive water balance; (2) maximal conservation of water with the elaboration of urine of a maximal concentration; and (3) a considerably negative salt balance with totals of 600 milliequivalents of chloride and 800 milliequivalents of sodium per cent. Further observations made during the development of serum hypertonicity revealed an incapacity to produce a maximally concentrated

urine in the presence of a mounting tonicity of the serum. These observations indicate that the development of this syndrome is caused by a relative incapacity to conserve water or produce urine of appropriate concentration in association with the retention of a considerable amount of salt. This combination of observations may be explained by the inadequate formation of antidiuretic hormone, in consequence of progressively decreasing sensitivity of the afferent arm in the neurogenic antidiuretic reflex. In consequence of this progressive decrease in sensitivity, the formation of antidiuretic hormone—even though it continued—became cumulatively inadequate. The danger of water-deprivation and the reduction of its volume possibly initiate the secretion of a salt-retaining hormone, perhaps via the adrenal glands. — M. F. Levitt, M. Belsky and D. Polimeros: *Ann. Int. Med.*, 50: 788, 1959.

THE THERAPY OF TYPHOID FEVER

A comparison between the various modern methods of treating typhoid fever has been carried out by Professor C. F. Colucci of Naples on a series of 100 patients (*Presse méd.*, 67: 725, 1959). In this group 36 patients were treated with oral or parenteral prednisone for 18 days at the rate of 40 to 60 mg./day for the first 10 days, 20 to 40 mg./day for the next six days and 25 mg./day for the last two days (depending on the weight of the patient). In five cases of this group higher dosages called for by refractoriness of the disease were administered for 25 to 30 days. In 25% of these cases fever subsided by crisis in less than 24 hours; a failure was recorded in 6.6%; exacerbations took place in 23.3% but were usually controlled by reinstitution of treatment at the same or at a higher dosage with or without addition of chloramphenicol, and in 45% fever subsided by lysis in a period of three to ten days. A second group of 34 patients received oral or parenteral prednisone at the rate of 20 to 30 mg./day for seven days, 15 to 20 mg. for three days and 15 mg. for two days plus chloramphenicol 1-1.5 g./day for eight days and 1 g. daily for the balance of the treatment. In more than 50% of these cases fever subsided in less than

24 to 48 hours, the rest of the symptomatology followed suit and the patients went on to convalescence and definite cure in record time. Only 3.4% of cases sustained an exacerbation, which was promptly controlled. In the rest of the cases fever subsided by lysis in three to eight days. In the 30 patients who received only chloramphenicol in a dosage of 1 to 1.5 g./day for 10 days and 1 g./day for the balance of the treatment, fever disappeared by lysis in the majority of cases in five to seven days after the onset of therapy. In only 6.6% of cases was an exacerbation of symptoms noted after the original improvement; this was brought under control with reinstitution of antibiotic treatment. The majority of these 100 patients had been ill for periods of 10 to 20 days before onset of any of these forms of therapy and had received only symptomatic treatment in the meantime. No perforation was recorded in spite of prolonged treatment with glucocorticoid. In this respect the behaviour of the ulcerated ileum is markedly different from that of the ulcerated

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stomach or duodenum. Administration of synthetic glucocorticoids alone in the treatment of typhoid fever is less successful than that of chloramphenicol alone. Prednisone therapy did not interfere in any way with the rise in antibody formation. In the author's opinion the best treatment available at present is the combination of prednisone and chloramphenicol. The aim of this combination is to tone down the excessive organic reaction of the body and to achieve a gradual bacteriostasis which allows the development and mobilization of the organism's natural defences.

CORTICOSTEROID THERAPY OF RHEUMATIC DISEASE

The availability of corticosteroid hormones for the treatment of rheumatic diseases has provided the clinician with an important and efficacious mode of treatment, but it has also brought to the surface important theoretical and practical problems.

Case histories presented by Blechman and Vaughan (*Ann. Int. Med.*, 50: 571, 1959) serve to illustrate the fact that clinical suppression of symptoms may be of very short duration in some cases in which corticosteroids are used in the treatment of patients with active disease of refractory character. They also emphasize the dangers of gastro-intestinal haemorrhage, osteoporosis with compression fractures, intercurrent infections, psychotic episodes and the development of gangrene. Although it is not easy to demonstrate a primary causal relation between the administration of the hormones and the adverse reactions of the types mentioned, the frequency with which these reactions have been observed in patients under hormonal therapy indicates that the hormones at least constitute a contributing factor.

The diversity of these reactions is explained to a certain degree on the basis of the general suppressive effect of corticosteroids on anabolic metabolism; their usage results in the somatic expression of a catabolic state in the tissues, including those concerned with defence against infections. The general therapeutic principle they suggest is that corticosteroid therapy should be used only in pathological states in which disease

activity is likely to be comparatively brief, or in more chronic pathological states when the circumstances are obviously desperate. It should be pointed out that not all workers agree with these principles.

CAUSES OF LATE DIAGNOSIS OF CANCER OF THE LUNG IN MOSCOW

As in many other centres, the mortality from cancer of the lung in the hospitals in Moscow is

second only to that of cancer of the stomach, this lesion constituting 12.6% to 15% of all cancers. A study by Struchkov and Grigorian (*Khirurgiya*, 11: 30, 1958) is based on 400 patients with cancer of the lung, of whom 86% were diagnosed correctly in the out-patient service and 14% were admitted with other diagnoses. In 95.2% of those admitted with the correct diagnosis, the process was far advanced and in the group whose condition was not recog-

(Continued on page 68)

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Protamide is the therapy of choice for either early or delayed treatment, but early use assures greatest efficacy.

For example, in a 4-year study¹ and a 26-month study² a combined total of 374 neuritis patients treated with Protamide during the first week of symptoms responded as follows:

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PAGE 794

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1. Lehrer, H. W., et al.: *Northwest Med.* 75:1249, 1955.
2. Smith, Richard T.: *New York Med.* 8:16, 1952

MEDICAL NEWS in brief

(Continued from page 67)

nized before admission 90% had inoperable cancer. Eighty-three per cent of all patients had central cancer—that is, cancer which developed in the larger bronchi—and 17% had peripheral (bronchiolar) cancer. In 91.3% of all the patients, symptoms were those of the tumour in the lung whereas in 8.7% the symptoms were due to metastases in various organs and glands.

Lack of symptoms was the cause for delayed diagnosis in 49.6% of

the patients, although it is possible that some of these would have been discovered to have some symptoms if the history and investigation had been more carefully taken. In 78.8%, a doctor was consulted within one month, in 12.1% within three months, and in 8.1% within six months after appearance of first symptoms. Thus the majority consulted a doctor fairly early in the disease. The first visit to a doctor was to an internist of the out-patient department in 87.4% of cases and directly to a

radiologist in 5.3% of cases. During the three months after the first consultation, 95.7% of patients had a fluoroscopy only. As only 12.7% of all the patients who underwent fluoroscopy had the diagnosis established by this examination, it is obvious that this technique is unsatisfactory.

Before establishment of a correct diagnosis the majority of patients were being treated for chronic pneumonia (123 cases) and tuberculosis (82 cases). Of the series, 9.4% were sent to sanatoria and health resorts because of mistaken diagnosis of tuberculosis! The syndrome of minor symptoms was observed in 93% of 384 patients with the advanced form of cancer of the lung. These symptoms include fatigue, tendency to frequent influenza-like chest symptoms, fleeting neuralgic pains, and loss of weight. In summary, it can be said that 39.5% of the patients presented diagnostic problems, 10.9% delayed consulting a doctor in spite of symptoms, and in 49.6% of the patients the disease was asymptomatic. The authors appeal for a more thorough investigation of patients with chronic non-specific pneumonia, bronchiectasis, chronic abscess, chronic bronchitis and adenoma of the bronchus in order to uncover cases of pulmonary cancer at an earlier stage.



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GASTRIC PHYSIOLOGY AND PATHOLOGY

A recent issue of the CIBA Clinical Symposia (Vol. 11, No. 1, 1959) is devoted to a monograph on the physiology and pathologic physiology of the stomach by William H. Bachrach. Dr. Bachrach considers the nervous regulation of the stomach, its motor function and movements during the empty stage and during digestion, together with the physiology of gastric secretion, the effects of pyloric obstruction, total gastrectomy and diseases of the stomach and duodenum. The monograph is as usual lavishly supplied with visual aids.

GENERAL PRACTICE IN NORWAY

In a recent issue of the *Tidsskrift for den norske lægeforening* (79: 441, 1959) Iversen, a general

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MEDICAL NEWS in brief

(Continued from page 68)

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practitioner in private practice in the far north of the country, reports statistics of his work. The period of observation was 18 months, and the number of patients involved was 2700, with a slight preponderance of women. He classified illnesses according to the W.H.O. classification, and found that the biggest group was that of diseases of the respiratory organs, which comprised about 15% of all cases treated. Next in order came dermatological cases with 10%, disorders of the digestive system 8%, disorders of the locomotor system 8%, injuries and poisonings 6.4%, eye disorders 6.2%, consultations without a definite diagnosis 5.4%, symptomatic diagnosis 5%, diseases of the ear 4.7%, acute infections 4.6%, cardiovascular disease 4.5%, neuroses 3%.

In the group of respiratory disorders, the commonest conditions were acute upper respiratory infection, tonsillitis and acute bronchitis; abscesses, other skin infections, impetigo and eczema made up most of the skin diseases. There seems to have been a great deal of abdominal colic and diarrhoea, and the fact that many of his patients were heavy workers in mining perhaps accounts for the high incidence of pain in the back. The group listed as "consultation without a definite diagnosis" includes ante-natal cases, health examinations and immunizations. The commonest acute infection was whooping cough, with measles and oxyuriasis following. The commonest cardiovascular complaints were varicose veins and hypertension. Coronary disease seems to have been relatively rare.

Iversen is fully aware that an incidence of neuroses of only 3% is much lower than that commonly given for private practice, but he has applied the term only in cases where there was no definite complaint of somatic disorder, such as dyspepsia or headache.

It is often asserted that the general practitioner can deal with approximately 85% of all illnesses, and this is strikingly borne out in Iversen's figures for reference to specialists, for he found it necessary to refer 13% of all his cases. About 8% of the series had to be admitted to hospital.

Iversen notes that he worked a total of 506 days during this 18-

month period, and a total of 4128 working hours including 1375 on house calls. The average working day, including Sundays and holidays, was 8.3 hours; this is broken down into a 9.3-hour working day on weekdays and a 2.7-hour working day on Sundays and holidays. The hardest month was March and the lightest month May. The average number of consultations daily was 16.4, with a range from 9.3 to 21.1. The average number of house calls per day was 1.4, with a range from 0.8 to 1.8. His net income over this 18-month period was approximately \$10,000.

PULMONARY ABSCESS: A STUDY OF 70 CASES

Of 70 cases of pulmonary abscess treated at a veterans' hospital, 44 were treated medically and 26 surgically. There were 12 deaths, representing a mortality of 17.1%. Reporting this series Pickar and Rudoff (*J. Thoracic Surg.*, 37: 452, 1959) consider pulmonary abscess to be primarily a medical problem. They feel that operation should be performed, however, if continued radiological and clinical improvement under medical therapy cannot be demonstrated, if carcinoma is suspected, or if complications exist or develop which are considered surgical.

Cultures of the sputum, including sensitivity studies of the organisms, should be made immediately. These studies should be repeated at weekly intervals in order to be certain of the antibiotic sensitivity of the offending organism. This is particularly true in cases in which the infection is caused by *Staphylococcus aureus* or Friedländer's bacillus.

Although the prognosis in pulmonary abscess has improved with the advent of antibiotics and the development of improved anaesthesia and surgical techniques, it continues to be a prolonged morbid process with a substantial mortality rate.

GROUP THERAPY FOR JUVENILE DELINQUENTS

How to restore juvenile delinquents to normal life by means of group therapy and group work was discussed in Sweden last August when some 70 experts from Europe, the U.S.A. and Canada gathered at Sigtuna, near

Stockholm, for the eighth meeting arranged by the International Union for Child Protection and the International Save-the-Children Fund. The increasing extent of juvenile delinquency, which is now almost universal, is forcing society to find new methods for the treatment of young criminals. Group therapy of juvenile delinquents was introduced some ten years ago when the International Union for Child Protection started scientific study of the method. The delegates were almost unanimously agreed that so far group therapy has proved successful, although nothing definite can yet be said about the method, since it is still in an experimental stage. Group therapy and group work have the advantage of being much less expensive than individual treatment. — Swedish-International Press.

HEALTH LEVELS IN ADVANCED NATIONS

Four nations which have achieved levels of health among the highest in the world are the United States, England and Wales, Sweden and France. These four countries also maintain health statistics which are easy to compare internationally. The September 1959 issue of *Progress in Health Services* (Vol. 8, No. 7), published by the Health Information Foundation of New York, contains a brief study of health levels in these four nations between the years 1901 and 1958.

The expectation of life at birth was highest in Sweden and has remained so, but the expectation of life at birth in England and Wales has advanced slightly more than that in the United States during the last 60 years. However, differentials in life expectancy between the countries are narrower than formerly, and any further sizeable increase in life expectancy will depend on major success in dealing with cardiovascular-renal disease, cancer or accidents.

In all countries, the decline in mortality has been greatest for younger persons and least for older. The gap of mortality between males and females has increased greatly since 1900; in that year male mortality rates exceeded female by about 15%, whereas now they exceed female rates by over 50%. This change is due not

(Continued on page 72)



ANAESTHETIC NEWS

The history of anaesthesia

PART I

From Adam to Humphrey Davy

Every minute of the day, in hospitals the world over, surgeons and anaesthetists perform intricate and critical operations. Their patients are old and young, healthy and totally infirm . . . but their lives are protected and extended immeasurably by modern science.

Through research, the science of anaesthesia has reached a high standard of perfection. It might be said that its origin can be traced even to the beginning of the world and the creation of Eve when, the Bible says: "And the Lord God caused a deep sleep to fall upon Adam, and he slept".

The early centuries are spotted only with the occasional mention of relief of pain in the form of anaesthesia. A Babylonian clay tablet describes the use of herb drugs as an anaesthetic in 2250 B.C. Throughout the Middle Ages many attempts were made to alleviate pain, mainly involving "black magic" and very little logic. It was not until 1513 that the first practical method was attempted. During that year, monks used a method of inhaling alcoholic fumes to ease suffering prior to and during surgical intervention. However, over two centuries elapsed before the first dependable means replaced these early efforts.

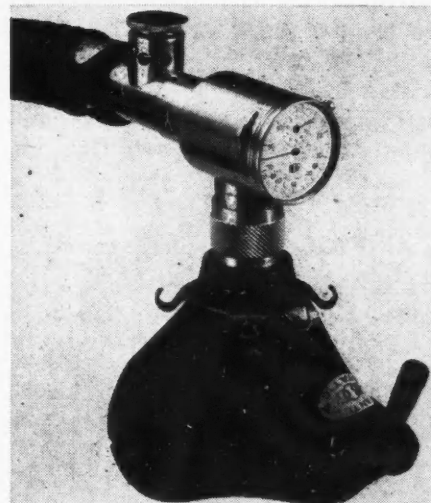
Until the experiments of Joseph Priestley there were isolated cases of partial success, but it was the discovery of carbonic acid gas, oxygen and nitrous oxide in 1771 and 1772 that actually led to anaesthesia as we know it today.

Priestley's experiments led to the first apparatus to be designed for the administration of nitrous oxide. The machine was fabricated by Humphrey Davy in 1779. Davy's first experiments with this gas encouraged many others to further discoveries. For instance, William Allen, lecturer on Chemistry at Guy's Hospital, wrote in his diary in March, 1800:

"Present, Astley Cooper, Bradley, Fox and others. We all breathed the gaseous oxide of azote. It took a surprising effect upon me, abolishing completely at first all sensation; then I had the idea of being carried violently upward in a dark cavern with only a few glimmering lights.

The company said that my eyes were fixed, face purple, veins in the head very large, apoplectic stertor. They were all much alarmed, but I suffered no pain and in a short time came to myself."

After these early experiments, success was followed fast by further success. Anaesthesia, and the equipment to administer it, was developed through the centuries until it reached the high standards of the British Oxygen Company products of today. But it does not stop here. Every year new discoveries, through continuing research, lead to further perfection of the B.O.C. Boyle Machine and anaesthetic sundries. Our part in the struggle for health and longevity is continuous in the provision of the finest anaesthetic equipment and medical gases . . . and our most important product . . . **DEPENDABLE SERVICE.**



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MEDICAL NEWS in brief

(Continued from page 71)

to increased mortality among males but to a more rapid decrease in mortality among females. Maternal and infant mortality rates were still lowest in Sweden. Falls in mortality rates are of course mainly due to the degree of control achieved over communicable diseases. In the cardiovascular-renal category, rates for some conditions such as nephritis have remained stable or declined, but impressive increases have occurred, particularly in arteriosclerosis and coronary artery disease. Heart disease now accounts for 38% of all deaths in the U.S.A., 30% in Sweden and England and 16% in France. Cancer has also risen in importance as a cause of death, mainly as a result of a spectacular increase in respiratory cancer. England now exceeds the other countries in respiratory cancer mortality by a considerable margin of 31 per 100,000 against 18 for the U.S.A., 15 for France and 9 for Sweden. Mortality from motor vehicle accidents is about twice as high in the U.S.A. as in England and Sweden and about one-third higher than in France.

AMERICAN COLLEGE OF CHEST PHYSICIANS ESSAY CONTEST

The American College of Chest Physicians is offering three cash awards to winners of the 1960 Prize Essay Contest. The first prize is \$500, the second \$300, and the third \$200. The contest is open to undergraduate medical students throughout the world. Essays may be written on any phase of the diagnosis and treatment of chest diseases (cardiovascular or pulmonary). The contest will close on April 1, 1960. For application form and further information: American College of Chest Physicians, 112 East Chestnut St., Chicago 11, Illinois.

NEW AGENCY FOR SCHIZOPHRENIA

The formation of a United States voluntary health agency to mobilize public support for research in schizophrenia was announced on September 24. The president of this new organization

known as RISE, Inc. (Research in Schizophrenia Endowment) is Mrs. Godfrey S. Rockefeller. The sole purpose of the new agency is to advance research into the cause, treatment, prevention and cure of schizophrenia. The scientific council is headed by Dr. David M. Rioch, Director of the Division of Neuropsychiatry, Walter Reed Army Institute of Research, Washington, D.C. Vice-presidents are Dr. Stanley R. Dean

of Stamford, Conn., and Dr. Paul H. Hoch, New York State Commissioner of Mental Hygiene. Offices are at 9 Rockefeller Plaza, New York City.

BLOOD COAGULABILITY IN ISCHÆMIC HEART DISEASE

Previous work by McDonald and Edgill indicated hypercoagulability of the blood in the presence

improves hearing

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In patients with disturbances of the inner ear, Arlidin produced remission of their chief complaint (impaired hearing, tinnitus or vertigo) in over 50% of cases. "Significant hearing improvement" occurred in 32 of 75 patients.¹ Rubin and Anderson¹ attribute these symptoms of circulatory disorders of the inner ear to "labyrinthine artery insufficiency" due to spasm or obstruction of the vessels. They presumed that improvement could be produced by an agent capable of increasing blood flow and consider that the efficacy of Arlidin in this condition is due to its superior vasodilating and vasorelaxant effects.

1. Rubin, W., and Anderson, J. R.: *Angiology*, Oct. 1958.

of ischaemic heart disease. These findings created new questions which a recent study (*Lancet*, 1: 1115, 1959) attempts to answer. Twenty-two healthy men and 30 men with angina pectoris on exertion were compared with seven patients with acute coronary insufficiency and 10 with cardiac infarction. Repeated out-patient tests were also made on 15 healthy men and 29 men with angina pectoris on exertion.

The results confirm increased coagulability of the blood in patients with angina pectoris compared with normal subjects and show a further increase in patients with cardiac infarction. Patients with acute coronary insufficiency showed a level of coagulability nearer that of angina pectoris on exertion, and not as accelerated as that in cardiac infarction. Three possible reasons are mentioned for hypercoagulability after cardiac

infarction. The phase of hypercoagulability may precede infarction, initiate coronary thrombosis and persist afterwards. Hypercoagulability may merely be an expression of the presence of recent thrombosis, or it may be due to tissue damage and intravascular stasis. The authors are investigating the possibility of heparin deficiency or over-utilization.

POLYPS OF THE COLON AND RECTUM

In Chicago a long-term follow-up program has been undertaken, involving by now 9669 people who had undergone proctoscopic and x-ray survey as part of routine gastro-intestinal examination in a period of six years (1947-1952). In their latest report on the program, Rider *et al.* (*J. A. M. A.*, 170: 633, 1959) state that 537 patients were discovered to have polyps of the rectum or colon, and an attempt was made to re-examine each of these patients during the following years. Generally co-operation of the patients was good, 92.7% having at least one follow-up examination. The cost of the program is estimated to have amounted to some \$195 per original patient, and it is indicated that such low (sic) cost rates would not be possible in future follow-up projects. The formation of new polyps and the relationship of polyps to carcinoma are discussed, and data presented on 56 patients whose polyps were originally diagnosed as carcinoma *in situ*. Eight of the 24 patients who subsequently developed polyps and who were found to have frank carcinoma are described in some detail. Of the 70 deaths in the total series, 32 were due to carcinoma but only 16 of these lesions were in the colon. As a group these patients were found to be "polyp-prone" and to have a higher incidence of carcinoma of the colon than the general population without polyps. The subsequent incidence of carcinoma in the 372 patients who were followed up in the 4-9 years' study was lower than the incidence found at the beginning of the study, indicating that the local treatment—that is, prompt removal of polyps—may have a preventive value. It is recommended that patients with

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(Continued on page 74)

MEDICAL NEWS in brief

(Continued from page 73)

polyps should be examined annually until findings of at least five consecutive proctosigmoidoscopic and x-ray examinations of the rectum and colon have been negative.

TRYPTOPHAN METABOLISM AND MENTAL DISEASES

The results obtained by Price, Brown and Peters (*Neurology*, 9: 456, 1959) indicate that certain psychotic patients fail to metabolize kynurenine and 3-hydroxykynurenine in a normal manner. These two substances are tryptophan metabolites, and abnormally large amounts of similar products were excreted in the urine of these patients after ingestion of a loading dose of tryptophan. In animals such abnormality of tryptophan metabolism indicates a functional deficiency of pyridoxine. Drugs capable of antagonizing vitamins such as isoniazid have been shown to produce convulsions in some animals. A number of symptoms

of porphyria have been seen in patients with disturbed pyridoxine metabolism. Although this abnormality of tryptophan metabolism suggested a functional pyridoxine deficiency in these psychotic patients, neither biochemical nor clinical improvement followed pyridoxine supplementation. Chelating agents were, however, often observed to produce both clinical and biochemical improvement.

INSTITUTE FOR ADVANCEMENT OF MEDICAL COMMUNICATION

The Institute for Advancement of Medical Communication, New York City, has been awarded a grant by the National Science Foundation for a study of "The metabolism of new scientific investigation". The chief aim of this project is to investigate the processes by which new information becomes generally available to the scientific community. Richard H. Orr, M.D., executive

director of the Institute, will serve as principal investigator.

GRANTS FOR HEART RESEARCH

Out of a total of \$1.2 million allocated this year for heart research by the Life Insurance Medical Research Fund of New York more than \$130,000 has been allotted to eight projects in Canada, it has been announced by the Canadian Life Insurance Officers Association. In addition to these heart research grants, postdoctoral fellowships have been awarded to eight young Canadians to enable them to become qualified as heart researchers. They will work for the next year or two under the guidance of experienced scientists at leading research centres. These fellowships carry awards varying from \$4000 to \$5900.

The grants-in-aid to institutions are as follows:

Hôtel-Dieu Hospital, Montreal, for research by Dr. Jacques Genest on the mechanism and treatment of human arterial hypertension.



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1. The Food Exchange Lists referred to are based on material in "Meal Planning with Exchange Lists" prepared by Committees of the American Diabetes Association, Inc. and The American Dietetic Association in cooperation with the Chronic Disease Program, Public Health Service, Department of Health, Education and Welfare.

McGill University Faculty of Medicine, Montreal, for study by Dr. G. C. McMillan of the chemical nature and break-up of fatty substances in the blood which may have a bearing on the origins of atherosclerosis in particular and several forms of heart disease in general.

McGill University Faculty of Medicine, Montreal, for research by Dr. Inge Dyrenfurth on aldosterone secretion rates and metabolism.

University of Alberta Faculty of Medicine, Edmonton, for research by Dr. Cyril M. Kay on muscle proteins and the conversion of fibrinogen to fibrin. This is the general and continuing study of specific body chemicals that regulate blood clotting.

University of British Columbia Faculty of Medicine, Vancouver, for research by Dr. P. Constantini on heparin-like substances to determine if their ability to reduce fat content of human blood is applicable in the prevention or the treatment of heart disease caused by hardening of the arteries.

University of British Columbia, British Columbia Research Council, Vancouver, for research by Dr. H. G. Khorana on the chemistry and enzymology of polynucleotides.

University of Western Ontario Faculty of Medicine, London, for study by Dr. Alan C. Burton of the physical properties of blood flow under varying conditions.

University of Western Ontario Faculty of Medicine, London, for study by Dr. K. K. Carroll of the relation of erucic and nervonic acids to sterol synthesis of the chemical components of the human production of various substances related to the regulation of hormones. Hormones are under investigation in the search for causes and possible treatment of hypertension.

Postdoctoral Fellowships

James Q. Bliss, M.D., of Kingsville, Ont., for study with Dr. Peter L. Krohn at the University of Birmingham, England; Jaroslav V. Frei, M.D., of Montreal, for study with Dr. A. C. Ritchie at

McGill University, Montreal; James Alan Herd, M.D., of Vancouver, for study with Dr. Eugene D. Robin at Harvard Medical School, Boston; Joseph A. Hinke, M.D., of Vancouver, for study with Prof. B. Katz at University College, London; Bernard J. Leboeuf, M.D., of Montreal, for study with Dr. Albert E. Renold at Harvard Medical School, Boston; Nico M. van Gelder, Ph.D., of Montreal, for study with Dr. J. H. Gaddum at the Institute of Animal Physiology, Cambridge, England; Serge Renaud, V.M.D., of Montreal, for study with Prof. Hans Selye in the Institute of Experimental Medicine and Surgery, University of Montreal; Tom Webb, Ph.D., of Toronto, for study with Prof. P. Grabar at the Institut Pasteur, Paris.

PORTAL HYPERTENSION AND THE ABSENCE OF OBSTRUCTION

It has become a truism to ascribe portal hypertension to either intrahepatic or extrahepatic obstruction.

(Continued on page 76)

Important

Successful reducing requires the cooperation of both patient and physician. As a patient you need to have your diet specially adjusted to your specific reducing goal. Your physician needs to have objective evidence of your weight status in order to evaluate your progress. The chart outlined below is designed to aid both aims.

PHYSICIAN—please fill in data at start of diet, height and optimum weight for build, calorie level of diet, and number of pounds to be lost per week.

PATIENT—please fill in all other information, making sure to use same scales for each weekly weighing. It is not desirable to check weight every day.

YOUR CHECK-UP CHART

Date at beginning of diet: _____ Calorie level of diet: _____
 Number of pounds to be lost per week: _____ Height: _____ Optimum weight for build: _____

WEEKS	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
WEIGHT (POUNDS)																	
DIET																	
DOCTOR																	

* Note personal chart to be filled in by physician and patient. Serves as constant reminder to patient to persist with diet.

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MEDICAL NEWS in brief

(Continued from page 75)

However, this attitude tends to ignore the hydrodynamic of intraluminal pressure which depends not only on the resistance to the flow but also on its volume. Within the past ten years Tisdale, Klatskin and Glenn of New Haven, Connecticut, have encountered at the Grace—New Haven Community Hospital five patients with bleeding oesophageal varices and portal hypertension in the absence of demonstrable intrahepatic or extrahepatic venous obstruction. The case histories of four of them are presented in the *New England Journal of Medicine* (261: 209, 1959). The first of these patients whose cases are presented is a 23-year-old single man who had massive hæmatemesis and who at operation was found to have a portal vein pressure of 315 mm. of saline solution. A splenoportogram and a careful inspection at laparotomy demonstrated a patent, somewhat dilated portal system with signs of definite elevation of portal pressure. The second patient

was a 58-year-old man also suffering from massive hæmatemesis, whose portal venous pressure fell from 320 to 119 mm. of saline after establishment of an end-to-side portacaval anastomosis. This man had large oesophageal varices which appeared on radiological examination to be the only site of bleeding from the upper gastrointestinal tract. The third case was that of a 72-year-old man, also presenting with massive hæmatemesis, whose portal vein pressure was 230 mm. of saline. Although he survived the operation, he developed heart failure and died on the 14th postoperative day. Post-mortem examination showed a marked dilatation of the entire portal venous bed, but no evidence of thrombosis at any point. The last case was that of a 10-year-old Negro girl who had also vomited blood and in whom a pressure of 375 mm. of saline was recorded in the gastroepiploic vein. This girl had a palpable spleen, but showed no evidence of obstruction to the portal outflow either outside or within the liver. It should be pointed out that the liver in

all these cases was normal in size and consistency and that there were no other manifestations of liver disease.

Moreover, radiographic visualization failed to reveal any evidence of narrowing, occlusion or cavernous transformation of the splenic or portal vein. As stated earlier, it is theoretically possible that an increase in the volume of blood entering the portal system may lead to sustained portal hypertension. According to Womack and Peters, the bowel wall contains arteriovenous anastomoses which are humerally controlled and help to determine the degree of oxygenation of portal blood. It is conceivable that the volume of blood flowing through the portal system could be increased by this mechanism. In the words of the authors, "Although gross arteriovenous anastomoses involving the splenic and portal veins were not found, functional or structural alterations of the vessels of the gastrointestinal tract, spleen and the liver may have permitted increased flow of blood into the portal vein, with a resultant rise in pressure. Despite



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Recent clinical research emphasizes the growing usefulness of low sodium diets in a number of critical conditions. You can save much time and repetitious talk by employing the new Knox Low Salt Brochure for all patients needing the benefits of a low sodium intake. Diets are based on Food Exchanges¹ and can be easily individualized by selecting one of three caloric levels—1200, 1800 and unrestricted—and by arranging sodium intake at levels of 250, 500 or 1,000 milligrams per day. Separate bibliography of 53 late references available on request.

1. The Food Exchange Lists referred to are based on material in "Meal Planning with Exchange Lists" prepared by Committees of the American Diabetes Association, Inc. and The American Dietetic Association in cooperation with the Chronic Disease Program, Public Health Service, Department of Health, Education and Welfare.

the compensatory dilatation of the main portal vessels and the opening of numerous venous collaterals, portal pressures remained elevated, with the eventual production and rupture of oesophageal varices."

RADIOACTIVE ROSE BENGAL IN LIVER FUNCTION TESTING

The rate of disappearance of radioactive rose bengal from the blood can be determined by external scintillation over the lateral part of the head. Disappearance rates of rose bengal as measured in blood and by head counts closely paralleled each other in the normal, and reproducibility of the tests in the fasting state in the normal and in patients with pathological liver conditions was consistently good. Food caused considerable variations, usually in the direction of increased blood retention of dye. The test can be carried out in patients with jaundice, as it does not depend on colour changes; it was found to show good correlation with the

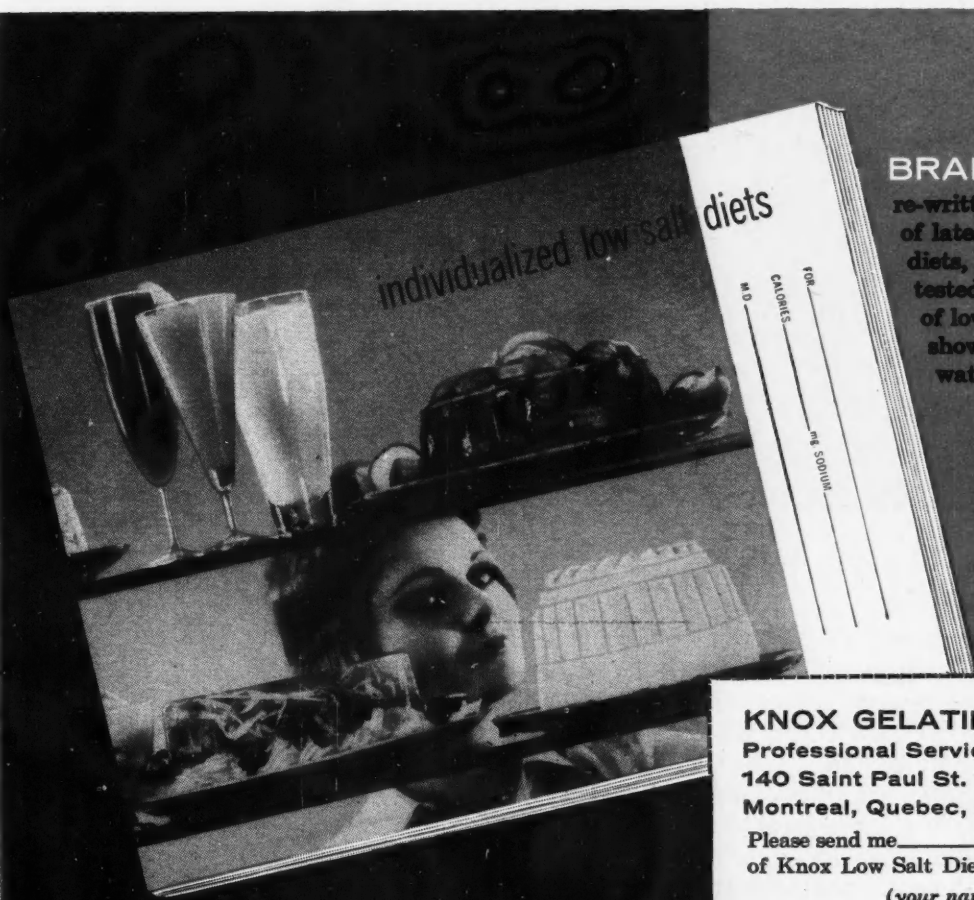
sulfobromophthalein test. On the basis of their experience in 105 patients with various liver diseases and comparison with normal subjects in their study, Nordyke and Bland (*J. A. M. A.*, 170: 1159, 1959) recommend this as a sensitive test of liver function.

INTRACRANIAL CHORDOMA

Chordomas are rare tumours derived from the notocord. About half of them are found at the sacrococcygeal level and a little less than the remainder develop inside the skull. They then arise in the region of the clivus blumenbachii about 1 cm. posterior to the dorsum sellæ. Demir and Steegmann of Kansas City (*Neurology*, 9: 514, 1959) describe an intracranial chordoma which was discovered in a 44-year-old man complaining of severe occipital headaches. This symptom was promptly followed by diplopia and internal rotation of the left eye. The diagnostic problem presented by intracranial chordomas is exemplified by the fact that lead

intoxication was suspected at first. However, physical examination revealed bilateral sixth nerve weakness with unsustained horizontal nystagmus, a slight left lower facial weakness and sluggish pharyngeal reflexes. Most of the usual laboratory tests were normal, cerebrospinal fluid pressure was 170 mm. and the only abnormality was a cerebrospinal fluid total protein level of 54 mg. %. A radiograph of the skull showed erosion of the floor of the middle fossa. The roof of the sphenoid could not be identified, and on one side the basilar foramina appeared wiped out. The anterior clinoids were practically gone or appeared as a shell. Biopsy of the nasopharynx supplied information of a negative nature. A diagnosis of middle fossa tumour was considered most probable. The patient was discharged without any treatment but was soon readmitted with a recrudescence of symptoms. A pneumoencephalogram revealed a soft tissue mass that extended from the cisterna chiasmatica back to the level of the cisterna inter-

(Continued on page 78)



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MEDICAL NEWS in brief

(Continued from page 77)

peduncularis. This mass was thought to be a pharyngeal tumour that had invaded the middle fossa. A course of roentgen therapy was instituted but failed to produce any improvement. The patient died 13 months after his first hospitalization. At autopsy, a tumour was found lying at the base of the brain, anterior to the pons and spreading into the sella turcica, the paranasal sinuses and the region of the nasopharynx. The sella turcica was almost completely destroyed and no pituitary tissue could be recognized. This mass was grey to white in colour, of variable consistency and measuring 6x5x4 cm. It was circumscribed and well encapsulated, composed of gelatinous masses or islands of grey tissue and oozing sticky mucoid material on the cut surface. The histological appearance varied in different areas from solid regions to others composed mostly of physaliferous cells and cystlike formations filled with mucinous material. It was relatively

avascular, and granulations staining deep red found in certain cells were found to be made up of glycogen. Most of the lesions seen in the rest of the brain could be ascribed to destruction of tissue from compression by the tumour. The authors state that a chordoma should be suspected when bone destruction or soft tissue mass is visualized in the spheno-occipital and hypophyseal areas in the midline, since most of these tumours arise in the region of the clivus. These tumours have been reported in either sex and at any age, but seem to be most common in the third and fourth decades.

NATIONAL CANCER INSTITUTE RESEARCH FELLOWSHIPS

The National Cancer Institute of Canada offers a number of Research Fellowships. They are designed to provide advanced training and experience in cancer research for individuals who plan a career in which furthering knowledge about cancer will be a major interest. These Fellowships are not

awarded for the purpose of providing practical clinical training (Clinical Fellowships are provided by the Canadian Cancer Society).

Fellowships are open on equal terms to men and women and are awarded to the applicants who are deemed best qualified on the evidence submitted.

A candidate must be a graduate of a university approved by the Institute. Research Fellowships are normally tenable in Canada.

The value of Fellowships will depend on the training and experience of the candidate.

Tenure and payment of a Fellowship shall normally commence on April 1 or July 1.

Application for a Fellowship must be made by the candidate to the National Cancer Institute of Canada on an official form on or before December 15 of the preceding year.

A copy of the regulations concerning these Fellowships together with application forms may be obtained from the National Cancer Institute of Canada, 800 Bay Street, Toronto 5, Ontario.



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1. Kirsner, J.B.: J.A.M.A. 166:1727, (April 5) 1958.

THE SHOULDER- ARM SYNDROME

In a symposium read before a section of the American Medical Association, J. W. Pender of Palo Alto, California, discussed some basic concepts of the shoulder-arm syndrome. He stressed the difficulty of diagnosis which is due to several reasons, the main being that signs and symptoms are not always characteristic and that the syndrome is almost always associated with other diseases and disabilities. The patient frequently becomes discouraged because of the prolonged treatment and seeks new advice and is thus lost to the physician who originally saw him. The need for excluding all other possible disease which might be causing sympathetic dystrophy is emphasized; for instance, incompletely reduced dislocation, ununited fracture, or a neuroma may be the primary cause. Teamwork between the internist or surgeon and the anaesthesiologist, physiatrist, or psychiatrist contributes greatly to the accuracy of the diagnosis. The most useful test

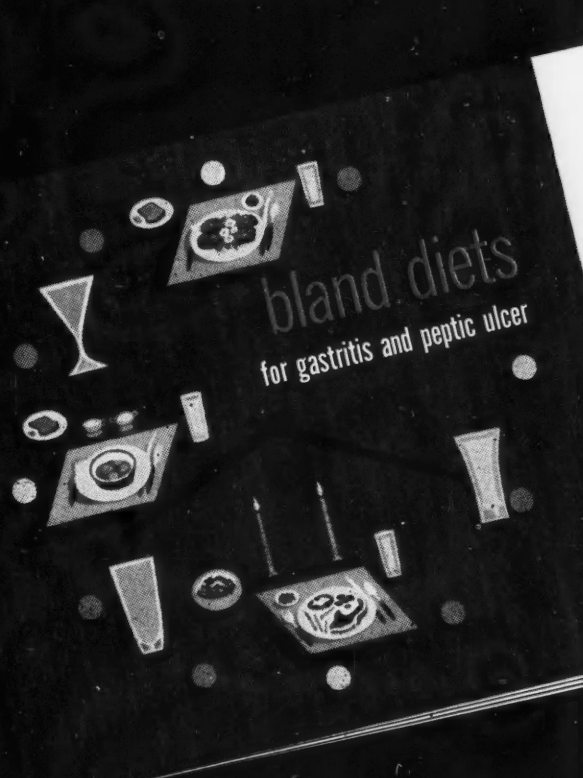
in the diagnosis of the syndrome is injection of a short-acting anaesthetic agent into the stellate ganglion on the same site as the disability. If relief follows the injection, this is good evidence that sympathetic dysfunction contributes to the disability. Pender postulates that the original disability invokes an alarm reaction and causes an increased sympathetic outflow. If this is blocked long enough to allow the underlying lesions in the extremity to heal, the cycle is broken and the patient recovers. The earlier in the course of the syndrome this treatment is carried out, the more successful it will be.

The psychological component of the syndrome is of equal if not greater importance, and the successful physician will exhibit a personal interest in this patient and win his confidence. This is particularly important when treatment is prolonged and progress is slow. The will on the part of the patient to get well has to be developed and in cases of compensation for injury the patient has to be taught

not to fear the loss of this economic support. Although the psychiatrist is better trained to handle these problems, the surgeon and the internist or the anaesthesiologist and physiatrist have the same opportunities for successful treatment by both attacking the physiological component and offering the patient interest, sympathy and encouragement.

Neurological involvement causing pain in the shoulder and the arm was discussed by P. C. Bucy and H. R. Overhill of Chicago. Disease involving the vertebral column is most frequently herniated cervical intervertebral disc, and the methods of diagnosing as well as the treatment were reviewed. Bucy and Overhill do not believe that most of these patients should be operated on, as they found that 80-85% can be relieved by conservative treatment. Continuous cervical traction with 5-10 lb. for some 10-14 days and then immobilization of the neck in a plastic collar is their treatment of choice. If this does not provide fairly prompt im-

(Continued on page 80)



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MEDICAL NEWS in brief

(Continued from page 79)

provement and if the condition has been present for more than a few weeks or has been recurrent, the offending herniated cartilage should be removed. Spinal cord tumours, involvement of the brachial plexus by trauma, tumours of the lung, cervical ribs, spasm of the scalenus anterior muscle, and aneurysms of the subclavian artery were also discussed and their diagnostic features illustrated by several case reports. Although rare, the involve-

ment of peripheral nerves by trauma or tumour has to be kept in mind.

Visceral causes of pain in the shoulder and upper extremity were considered by E. H. Morgan of Seattle. The absence of local objective findings in a painful shoulder leads the internist to seek elsewhere for the cause of pain, and persistent search may reveal such conditions as carcinoma of the lung and intrathoracic tumour with partial destruction of vertebræ. As remote sources of shoulder pain,

the diaphragm and phrenic nerves are most important. Morgan recalls experimental and clinical work by Capps and Coleman, who established that localization of pain principally in the trapezius ridge results from stimulation of afferent sensory fibres of the central portion of the diaphragm. This explains the author's experience with pulmonary infarction involving the diaphragmatic surfaces of the lung as an important common cause of shoulder pain. Cardiovascular, intra-abdominal and even genitourinary disease has to be considered in eliminating remote causes of shoulder arm pain. Pain of remote visceral origin rarely appears in the deltoid region, which is the common site of pain due to intrinsic disease of the shoulder.

J. T. Nicholson and H. S. Wieler, Jr., of Philadelphia discussed the local causes of pain, with particular reference to injuries of the tendinous capsular cuff, calcification of tendons, bicipital tendinitis, and "frozen shoulder". Early recognition of these conditions may prevent full development of the syndrome and result in early recovery. P. A. Nelson of Cleveland discussed the physical treatment of this condition. He divides the pathological conditions causing pain in the shoulder into those without and those with limitation of shoulder motion. When physical therapy is administered by a fully qualified therapist, it usually is effective. The most striking results are obtained in cervical radiculopathy and cervical thoracic outlet syndrome. In some cases of acute peri-arthritis and acute trauma to the shoulder, cold moist compresses or an icebag is applied. In peripheral neuropathy, local heat may make the patient more uncomfortable. Ultrasonic diathermy which has recently come into general use is helpful as an adjunct in treatment of peri-arthritis of the shoulder and causalgia. Patients should be cautioned not to use sun lamps for any length of time or electric pads on low setting for the night. Short circuits and serious burns have been known to occur. A hot water bottle or hydrocollator pack is preferred as a convenient and safe form of heat application in the home.—J. A. M. A., 169: 795-817, 1959.

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INSTANT POSTUM



MEDICAL NEWS in brief

(Continued from page 80)

**FACTORS INFLUENCING
THE PROGNOSIS OF
SYSTEMIC LUPUS
ERYTHEMATOSUS**

Clinical manifestations, duration of disease and causes of death in 33 fatal cases of lupus erythematosus were compared by McCombs and Patterson (*New England J. Med.*, 260: 1195, 1959) with similar data in 39 non-fatal cases of the disease. There were eight males in the whole series, of whom six died; of 69 females 32 died. The majority of women developed the disease during the menarche. Renal involvement carried the most serious prognostic significance, especially if accompanied by marked hypertension. Of 37 patients in this group 27 died; of the 10 living patients six have a very poor prognosis and only one patient shows significant improvement in renal function.

Of 30 patients who received corticosteroids only one developed renal disease at a later date, whereas of the 10 who did not receive corticosteroids three manifested renal disease. Of 11 patients who had clinically obvious pericarditis one also had uræmia. Two patients did not receive corticosteroids and both died, whilst of the eight remaining patients who received adequate steroid treatment all recovered. Only one of six patients with involvement of the peritoneum survived. Nine patients had obvious myocarditis; five who died were in the untreated group and four who recovered had received steroids. Of 12 patients with central nervous system involvement three died, although all of them received corticosteroids. One of the latter died of uræmia, whereas in the other two the corticosteroids were discontinued because it was believed that they were contributing to the development of psychoses. Haemolytic anaemia was present in seven cases and four of these patients died, but it is believed that other factors than the anaemia were important in them. Of four patients with thrombocytopenic purpura two died, one in heart failure and one of renal failure. A close relation between pregnancy and lupus erythematosus was present on 20 occasions in this series. Some women were found

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LEIGHTON SMITH, M.D.

The election of Dr. Leighton Smith as Vice-President of Ayerst, McKenna & Harrison Limited, is announced by E. Glyde Gregory, President. Dr. Smith, a graduate in Medicine from McGill University in 1943, practised in Montreal until 1951, when he was appointed Medical Director of Ayerst, McKenna & Harrison in Canada. Dr. Smith will continue to hold that position.

to go through pregnancy without difficulty, and all of those who successfully completed the pregnancy were free of renal disease.

The influence of corticosteroid therapy was carefully studied. Of 50 adequately treated patients on corticosteroids 18 died (36%). Twenty-five patients received no corticosteroids and 18 died within three years after the diagnosis was established. In five the disease was mild and did not progress, in one it has improved but not disappeared altogether, and one patient had a spontaneous remission but has evidence of renal insufficiency. Of the 32 patients who received corticosteroids and who were still alive when the study was concluded, 11 were in remission and did not require maintenance therapy and five of them had survived for more than three years. Twenty-one patients were on ACTH, cortisone or similar preparation. Renal lesions did not seem to be improved by corticosteroid therapy, as can be seen by the finding that of 21 patients on this treatment, with renal involvement at the time of diagnosis, nine died

of uræmia, four died of other causes and three had chronic uræmia.

**INFLUENCE OF
MYOCARDIAL INFARCTION
ON PLASMA-LIPOPROTEIN
CONCENTRATION**

Experiments were carried out by Dodds and Mills (*Lancet*, 1: 1160, 1959) to determine the average lipoprotein level in healthy men and in patients with myocardial infarction by using ultracentrifugal analysis, paper electrophoresis, and Cohn fractionation followed by determination of cholesterol levels. Normal data were obtained by analyzing samples from some 220 male volunteers of average age 56. Nineteen specimens were taken from men who had suffered from myocardial infarction some six weeks earlier, and in 78 patients (average age 58) in hospital for definite myocardial infarction samples were obtained where possible, 24 hours after the attack, three or four days later, and afterwards at intervals of seven days. Significant differences between the values for healthy men and for both groups of patients who had had coronary infarction were revealed.

Follow-up of the levels of the different components of the blood after myocardial infarction disclosed a profound disturbance of the equilibrium of lipoprotein metabolism after infarction. This causes their level to vary considerably from week to week and indicates that a single determination six weeks after infarction does not give a true measure of the lipid abnormality during the first two months of illness. It seems probable that in men less than 45 years old myocardial infarction is often preceded by lipoprotein abnormalities which become more evident after the attack. In elderly people a "normal" lipoprotein pattern is common before myocardial infarction. The authors conclude that in certain cases the blood lipoproteins are concerned in the development of coronary artery disease. The effect of the infarct itself on the lipoproteins has been ignored by many workers, and as a result lipoprotein analysis has received undue significance in some quarters and has been rejected undeservedly in others.

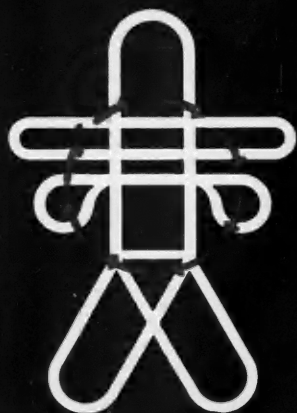
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ACTASE

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Fibrinolysin (Human)



1. Moser, K.M.: J.A.M.A. 167:1695 (Aug. 2) 1958.
2. Clifton, E.E.: J. Am. Geriatrics Soc. 6:118, 1958.
3. Sussman, B.J., and Fitch, T.S.P.: J.A.M.A. 167:1705 (Aug. 2) 1958.
4. Singher, H.O., and Chapple, R.V.: Clin. Med. 6:439 (March) 1959.